EUnetHTA Joint Action 3 WP4

**Rapid assessment of other technologies using the HTA Core Model®
for Rapid Relative Effectiveness Assessment**

SURGICAL PROCEDURES FOR TREATMENT OF OBESITY

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Disclaimer

The content of this assessment represents a consolidated view based on the consensus within the Authoring Team, it cannot be considered to reflect the views of the European Network for Health Technology Assessment (EUnetHTA), EUnetHTA's participating institutions, the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

Assessment Team

Authoring Team	Author(s)	Experts from Norwegian Institute of Public Health (NIPHNO) Norway
	Co-Author(s)	Experts from Health Information and Quality Authority (HIQA) Ireland, Austrian National Public Health Institute (GÖG) Austria* *GÖG joined the assessment team after completion of the planning phase
Dedicated Reviewer(s)		Experts from Agency for Health Quality and Assessment of Catalonia (AQuAS) Spain, French National Authority for Health (HAS) France, State Health Care Accreditation Agency (VASPVT) Lithuania
Statistician		Statistician from State of Health, Austria

Acknowledgements

Project Manager(s)	Member of Norwegian Institute of Public Health (NIPHNO) Norway
External Expert(s)	Dr. Tom Mala (obesity surgeon), Oslo University Hospital (OUS) Norway Dr. Rune Sandbu (obesity surgeon), Vestfold Hospital Trust (SIV) Norway Dr. Judith Aron-Wisnewsky (endocrinologist/nutritionist), Assistance publique (Paris hospitals) (APHP), Pitié Salpêtrière University Hospital, France Dr. Laurent Genser (obesity surgeon), Assistance publique (Paris hospitals) (APHP), Faculty of Medicine, Sorbonne University, France Dr.Juan José Yepes-Nuñez, GRADE NMA expert advisor, Universidad de Los Andes, Colombia

Manufacturer(s) (factual accuracy check)	None*
Patient(s)	None
Patient Representative(s)	None
Illustrator	Selma Flodgren (Norway)
Medical Editor(s) [v1.3]	Semantix (Norway)
Graphical Editor(s) [v1.4]	Manuela Kaitna (Austria)

* We reached out to the manufacturers to enquire if they produced any relevant medical device, such as gastric bands or rings, that was CE-approved. We did not receive expressions of interest to participate in the assessment from the manufacturers that we invited. Here below we list the invited companies: Allergan, Bariatric Solutions, Bariatec, Medtronic Covidien, Cousin Biotech, Helioscopie, Medical Innovation Development, Apollo Endo. We also reached out to Johnson and Johnson (Ethicon) who informed us that they discontinued the production of the medical devices of interest.

Conflict of interest

All authors, co-authors, dedicated reviewers, external experts (health care professionals) involved in the production of this assessment have declared they have no conflicts of interest in relation to the technology and comparator(s) assessed according to the EUnetHTA declaration of interest (DOI) form, which was evaluated following the EUnetHTA Procedure Guidance for handling DOI form (https://eunethta.eu/doi).

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Contact the EUnetHTA Secretariat EUnetHTA@zinl.nl with inquiries about this assessment.

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LIST OF ABBREVIATIONS

ADA	American Diabetes Association
AE	Adverse Event
AGB	Adjustable Gastric Banding
AQuAS	Agency for Health Quality and Assessment of Catalonia
BMI	Body Mass Index
BP	Blood Pressure
BPD-DS	Bilio-Pancreatic-Diversion with Duodenal Switch
B-SG	Banded Sleeve Gastrectomy
CI	Confidence Interval
CrI	Credibility Interval
D-RYGB	Distal Roux-en-Y Gastric Bypass
EFF	Effectiveness
EPOC	Effective Practice and Organisation of Care group
FPG	Fasting Plasma Glucose
GERD	Gastroesophageal reflux disease
HAS	French National Authority of Health
HbA1c	Glycated Haemoglobin
HDL	High Density Lipoprotein cholesterol
HIQA	Health Information and Quality Authority
HR	Hazard Ratio
HRQoL	Health Related Quality of Life
ICD	International Classification of Diseases
LDL	Low Density Lipoprotein cholesterol
MA	Meta-analysis
MD	Mean Difference
MeSH	Medical Subject Headings
MetS	Metabolic Syndrome
MI	Myocardial Infarction
MID	Minimally Important Difference
MMol	MilliMole
NIPHNO	Norwegian Institute of Public Health
NMA	Network meta-analysis
OAGB	One Anastomosis Gastric Bypass
QoL	Quality of Life
PICO	Population Intervention Comparison Outcomes
POP	Planned and ongoing Projects
PROSPERO	International prospective register of systematic reviews

RCT	Randomised Controlled Trial
REA	Relative Effectiveness Assessment
RR	Risk Ratio
RYGB	Roux-en-Y Gastric Bypass
SAF	Safety
SD	Standard Deviation
SMD	Standardised Mean Difference
SF-36	Short Form-36
SG	Sleeve gastrectomy
SR-RYGB	Silicon-ring Roux-en-Y Gastric Bypass
SUCRA	Surface Under the Cumulative Ranking Curve
TC	Total Cholesterol
TG	Triglycerides
VASPVT	State Health Care Accreditation Agency

SUMMARY OF RELATIVE EFFECTIVENESS OF OBESITY SURGERY PROCEDURES

Scope

This aim of this assessment was to determine the comparative effectiveness and potential superiority of different bariatric procedures for treatment of adult obesity in improving outcomes of importance for this group of people (e.g. weight loss, diabetes control, and HRQOL). The scope can be found here: Scope.

The research questions were as follows:

[D0001] – What is the relative effect of the different bariatric surgical procedures on mortality?

[D0005] – What is the relative effect of the different bariatric surgical procedures on weight loss, and diabetes control?

[D0006] – What is the effect of the different bariatric surgical procedures on progression of obesity including the development or worsening of comorbidities?

[D0012] – Do the bariatric surgical procedures differ in their effect on generic health related quality of life?

[D0013] – Do the bariatric surgical procedures differ in their effect on disease specific quality of life?

[D0017] – Do the bariatric surgical procedures differ in their effect on patient satisfaction?

Introduction

Obesity surgery, (also known as bariatric surgery, weight loss surgery or, in specific clinical circumstances, metabolic surgery) is the alteration of gastrointestinal anatomy and physiology using surgical methods with the aim of producing significant and sustained weight loss and resolution of, or improvement in, weight-related comorbidities, in particular type 2 diabetes (T2D) [B0001].

Traditionally, bariatric surgical procedures have been divided into restrictive or malabsorptive procedures, or a combination of both. Restrictive procedures decrease the capacity of the stomach thereby limiting the amount of food that can be consumed and include adjustable gastric banding (AGB) and sleeve gastrectomy (SG). Malabsorptive techniques limit the absorption of foods from the digestive tract by “bypassing“ a portion of the small intestine to varying degrees, depending on the procedure [B0002]. Biliopancreatic diversion with duodenal switch (BPD-DS), Roux-en-Y gastric bypass (RYGB), one anastomosis gastric bypass (OAGB), single anastomosis duodenal-ileal bypass with sleeve gastrectomy (SADI-S) and single anastomosis sleeve ileal (SASI) bypass can be defined as combination procedures, having both restrictive and malabsorptive mechanisms. In current clinical practice almost all bariatric surgical procedures are carried out laparoscopically.

All AGB products in clinical use should carry the CE mark and should be compatible with the gastric band used [A0020]. The manufacturers of AGBs including, Allergan, Bariatric Solutions, Bariatec, Medtronic Covidien, Cousin Biotech, Helioscopie, Medical Innovation Development, Apollo Endo and Johnson and Johnson (Ethicon) were contacted to confirm the regulatory status (CE marking) of identified devices. However, only one manufacturer replied, Johnson and Johnson (Ethicon), who have discontinued production of the REALIZE® adjustable gastric band.

Health problem

According to ICD-11, obesity is a chronic, complex disease characterised by the accumulation of excess adipose tissue that may impair health through the development of obesity-related comorbidities. Obesity is typically measured using the body mass index (BMI) at a population level.

The target population for this assessment is adults ≥18 years of age with a BMI ≥30 kg/m^2, specifically:

- BMI ≥40 kg/m^2, or
- BMI ≥35 kg/m^2 and comorbidities (for example, hypertension or T2D), or
- BMI ≥30 kg/m^2 and T2D who have not achieved durable improvements in glycaemic control with reasonable non-surgical methods.

Within Europe, obesity prevalence is variable between and within countries, and is influenced by factors such as age, gender or socioeconomic status. In 2016, across 18 European countries (including Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, The Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, and the UK) the estimated age-standardised obesity prevalence for those aged 20–84 years ranged from 22.7% in Portugal to 29.3% in the UK for men, and from 19.5% in Switzerland to 31.3% in the UK for women ([A0023]). Based on current trends, obesity rates are projected to continue to rise. Among the consequences of the rising prevalence of obesity is the associated rise in cardio-metabolic comorbidities such as hypertension, dyslipidemia and T2D and the associated burden on health care systems.

Selection of the most suitable intervention for an individual patient with obesity is dependent on the severity of the obesity, the presence of obesity-related comorbidities and lifestyle factors and is informed by a thorough clinical assessment ([A0024]). The treatment of obesity typically requires multicomponent lifestyle interventions including diet, physical activity and behavioural therapy. If treatment goals cannot be achieved or sustained with non-surgical methods, patients may be referred to specialist services such as bariatric surgery.

Methods

The material included in the TEC and CUR domain was identified in accordance with the published protocol. That is, information was obtained through scoping the literature, but no systematic search was undertaken. Where available, guidelines from professional societies or systematic reviews were used. Manufacturers of adjustable gastric bands were contacted to confirm the technical characteristics and regulatory status of identified adjustable gastric bands. Formal quality appraisal of the information in the TEC and CUR domains was not undertaken, however, the information was subject to internal review by dedicated reviewers and external experts in accordance with EUnetHTA processes.

After an initial search for existing evidence syntheses (e.g. systematic reviews, HTAs), we searched for RCTs in four electronic databases: Cochrane CENTRAL, Embase, MEDLINE, Web of Science. In addition, we searched for terminated, completed and published, completed and unpublished, and ongoing primary studies in ClinicalTrials.gov, WHO ICTRP, and EU Clinical Trials Register. We included only RCTs for both the safety and clinical effectiveness domain. A detailed search strategy is available in Appendix 1. We contacted manufacturers for additional published or unpublished studies. Two reviewers independently screened studies retrieved through the literature search against the predefined eligibility criteria. Data extractions executed by one reviewer, using a piloted form, were quality assessed by a second reviewer.

We used Bayesian network meta-analysis (NMA) to pool weight and diabetes outcomes. The study results were transformed to standardised mean differences (SMD). To incorporate long term effects, NMAs for 2 years, 3 years and 5 years follow-up were conducted. We report results derived from the fixed and random effects models. Ordinary meta-analysis was performed for other outcomes when feasible.

Risk of bias was independently appraised by two reviewers, using the Cochrane Risk of Bias tool [1]. The GRADE tool (Grading of Recommendations, Assessment, Development and Evaluation) was used to rate the certainty of evidence for each primary outcome [2]. We did not grade the secondary outcomes.

Results

Available evidence

Twenty-eight RTCs were included in this REA, and several companion studies (Table 9, Table A1) from the same trials. Twenty-two studies provided EFF data, and twenty-one of these studies, plus an additional six studies, provided data for the SAF domain. The assessment included seven main bariatric procedures (AGB, SG, RYGB, D-RYGB, OAGB, BPD-DS, and BPD), and two combined procedures (B-RYGB and B-SG). The comparisons were as follows: AGB vs RYGB (3 studies); AGB vs SG (1 study); SG vs RYGB (12 studies); D-RYGB vs RYGB (1 study); OAGB vs RYGB (2 studies); OAGB vs SG (1 study); BPD-DS vs RYGB (2 studies); BPD vs RYGB (1 study); B-RYGB vs RYGB (2 studies); B-SG vs SG (2 studies); B-RYGB vs SG (1 study). Most of the included studies were at overall high risk of bias. We also identified 24 relevant trial registry records including different obesity surgery procedures which were at different statuses (e.g. completed, ongoing, recruiting). The main reasons for excluding studies were no full text available, and/or wrong study design, population, type of intervention, or comparator.

The number of RCTs included in the NMA, treatments and patients for weight ranged between 11 studies, 8 treatments and 927 patients at 5 years follow-up, to 16 studies, 11 treatments and 2.288 patients at 2 years follow-up. The body of evidence for diabetes was considerably smaller and ranged from 5 RCTs, 5 treatments, and 455 patients at 5 years follow-up, to 6 studies, 6 treatments at 2 years follow-up and 666 patients at 3 years follow-up.

Clinical effectiveness

The results of the NMA for the specific bariatric procedures showed strong variations between the individual follow-up times, outcomes and whether the random effects or fixed-effect model was used. No treatment showed consistent superiority in the effect on weight and diabetes outcomes against other treatments. Overall, the treatments showed largely similar efficacy. The certainty of evidence for these results however was low to very low. HRQOL was improved after bariatric surgery, but with little to no differences between procedures (low to very low certainty of evidence). There was great uncertainty related to the estimations of expected number of early deaths (low certainty of evidence), and we could not determine whether the early (or late) deaths reported in the included studies were in any way related to hospital volume, the experience of surgeons, or the type of study site. Less than half of the included studies provided data for CVD risk reduction, and those that did, showed little to no difference between procedures. BPD-DS and D-RYGB however did show a greater effect on lipids than RYGB, but single studies provided data for these comparisons.

Safety

The results of this REA suggest a greater risk of GERD, and severe GERD requiring conversion surgery in patients with SG as compared to RYGB. Our results also suggest a greater risk of conversion surgery due to inefficient weight loss in AGB as compared to RYGB. The potential risk of metabolic complications was greater after the more malabsorptive procedures (BPD-DS, D-RYGB and OAGB) as compared to RYGB. Non-standardised classification and reporting of many of the other AEs hampered any attempts to analyse these further. It should be noted that a majority of the results were based on data from high risk of bias studies.

Upcoming evidence

We identified 9 on-going trials with planned publication date between 2022 and 2026. Five of these trials compared RYGB with SG, and four of these included only people with obesity and T2D. One trial compared OAGB with RYGB, and one SADI with RYGB (Table A25). There might be other relevant studies as well, i.e. studies that have their planned publication date in the past.

Table 1: Summary of findings table of obesity surgery – weight-related outcome – 2 years follow-up

Estimates of effects, credible intervals, and certainty of the evidence for comparison of bariatric surgery procedures for treatment of obesity

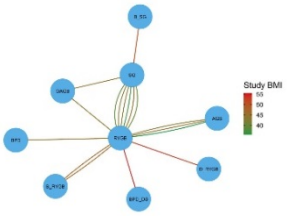
People: Adults with class II or class III obesity, with or without comorbidity

Settings: Bariatric clinics/hospitals

Interventions: AGB, SG, D-RYGB, OAGB, BPD-DS, BPD, B-RYGB, B-SG

Comparator: RYGB (SG)

Outcome: weight-related outcome at 2 years follow-up



Intervention procedure	Comparator procedure	No of studies (no of pts.)	NMA estimate SMD (95%CrI)	Absolute effect[§]	Quality of the evidence (GRADE)[†]
AGB	RYGB	3 studies (302 pts.)	0.47 (-0.85, 1.77)	60 fewer (516 fewer to 39 more)	⨁⊖⊖⊖ Very Low[a,b,c]
SG	RYGB	6 studies (1,329 pts.)	-0.27 (-0.83, 0.35)	29 fewer (144 fewer to 23 more)	⨁⨁⊖⊖ Low[a,b]
D-RYGB	RYGB	1 study (123 pts.)	0.18 (-1.14, 1.49)	18 fewer (389 fewer to 43 more)	⨁⨁⊖⊖ Low[a,b]
OAGB	RYGB	1 study (253 pts.)	-0.061 (-2.1, 1.94)	6 more (589 fewer to 49 more)	⨁⨁⊖⊖ Low[a,b]
BPD-DS	RYGB	1 study (60 pts.)	-1.56 (-3.4, 0.31)	47 more (35 fewer to 50 more)	⨁⨁⊖⊖ Low[a,b]
BPD	RYGB	1 study (40 pts.)	-0.02 (-2.36, 2.31)	2 more (726 fewer to 49 more)	⨁⊖⊖⊖ Low[d]
B-SG	RYGB	1 study (94 pts.)	-0.11 (-2, 1.75)	9 more (507 fewer to 49 more)	⨁⨁⊖⊖ Low[a,b]
B-RYGB	RYGB	2 studies (460 pts.)	0.85 (-1.78, 0.08)	142 fewer (493 fewer to 13 more)	⨁⊖⊖⊖ Very Low[a,b,c]
OAGB	SG	1 study (217 pts.)	-0.33 (-2.4, 1.8)	34 more (613 fewer to 78 more)	⨁⨁⊖⊖ Low[a,b]
B-SG	SG	NA	NA	NA	NA

† GRADE Working Group grades of evidence

High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different‡ is low.

Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different‡ is moderate.

Low = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different‡ is high.

Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different‡ is very high.

§ Based on an assumption that 95% of patients who receive RYGB achieve significant weight reductions (TBWL>20%) after two years

‡ Substantially different = a large enough difference that it might affect a decision

NMANMA-SOF-table definuition: ** Network metanalyses (NMA) reported as standardised mean differences (SMD), CrI: credible interval. Results are expressed in credible intervals as opposed to the confidence interval (CI) since a Bayesian analysis has been conducted.

Abbreviations: AGB: adjustable gastric banding; B-RYGB: banded Roux-en-Y gastric bypass; B-SG: banded sleeve gastrectomy; BPD: biliopancreatic diversion; BPD-DS: biliopancreatic diversion with duodenal switch; D-RYGB: distal Roux-en-Y gastric bypass; NA: data not availableOAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

Explanatory footnotes:

[a] Downgraded due to risk of bias limitations

[b] Downgraded due to imprecision.

[c] Downgraded due to inconsistency

[d] Downgraded twice due to imprecision

Table 2: Summary of findings table of obesity surgery – weight-related outcomes – 3 years follow-up

Estimates of effects, credible intervals, and certainty of the evidence for comparison of bariatric surgery procedures for treatment of obesity

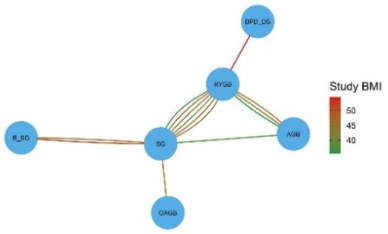
People: Adults with class II or class III obesity, with or without comorbidity

Settings: Bariatric clinics/hospitals

Interventions: AGB, SG, OAGB, BPD-DS, B-SG

Comparator: RYGB, SG

Outcome: weight-related outcome at 3 years follow-up



Intervention procedure	Comparator procedure	No of studies (no of pts.)	NMA estimate SMD (95%CrI)	Absolute effect[§]	Quality of the evidence (GRADE)[†]
AGB	RYGB	3 studies (289 pts.)	-0.67 (-2.44, 1.17)	55 more (340 fewer to 79 more)	⨁⨀⨀⨀ Very Low[a,b,c]
SG	RYGB	6 studies (781 pts)	-0.43 (-0.88, 1.73)	79 fewer (587 fewer to 63 more)	⨁⨀⨀⨀ Very Low[a,b,c,]
BPD-DS	RYGB	1 study (47 pts.)	1.53 (-5.09, 8.07)	502 fewer (920 fewer to 80 more)	⨁⨁⨀⨀ Low[a,b]
OAGB	RYGB	1 study (217 pts.)	0.67 (-5.28, 6.73)	147 fewer (920 fewer to 80 more)	⨁⨁⨀⨀ Low[a,b]
B-SG	RYGB	2 studies (144 pts.)	-0.25 (-2.89, 2.31)	28 more (771 fewer to 80 more)	⨁⨁⨀⨀ Low[a,b]
AGB	SG	1 study (80 pts.)	-1.1 (-3. 0.95)	134 more (355 fewer to 154 more)	⨁⨀⨀⨀ Very Low[a,b,c]
B-SG	SG	NA	NA	NA	NA

[†] GRADE Working Group grades of evidence

High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different[‡] is low.

Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different[‡] is moderate.

Low = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different[‡] is high.

Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different[‡] is very high.

[§] Based on an assumption that 95% of patients who receive RYGB achieve significant weight reductions (TBWL>20%) after three years

[‡] Substantially different = a large enough difference that it might affect a decision

NMANMA-SOF-table definuition: ** Network metanalyses (NMA)reported as standardised mean differences (SMD), CrI: credible interval. Results are expressed in credible intervals as opposed to the confidence interval (CI) since a Bayesian analysis has been conducted.

Abbreviations: AGB: Adjustable gastric banding; BPD: Biliopancreatic diversion; BPD-DS: Biliopancreatic diversion with Duodenal Switch; B-RYGB: Banded RYGB; B-SG: Banded Sleeve Gastrectomy; D-RYGB: distal Roux-en-Y Gastric Bypass; OAGB: One Anastomosis Gastric Banding; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve gastrectomy

Explanatory footnotes:

[a] Downgraded due to risk of bias limitations

[b] Downgraded due to imprecision.

[c] Downgraded due to incoherence

Table 3: Summary of findings table of obesity surgery – weight-related outcomes – 5 years follow-up

Estimates of effects, credible intervals, and certainty of the evidence for comparison of bariatric surgery procedures for treatment of obesity

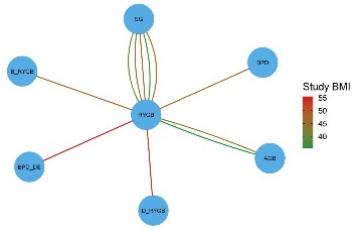
People: Adults with class II or class III obesity, with or without comorbidity

Settings: Bariatric clinics/hospitals

Intervention: AGB, SG, D-RYGB, BPD-DS, BPD, B-RYGB

Comparator: RYGB

Outcome: weight-related outcome at 5 years follow-up



Intervention procedure	Comparator procedure	No of studies (no of pts.)	NMA estimate SMD (95%CrI)	Absolute effect[§]	Quality of the evidence (GRADE)[†]
AGB	RYGB	2 studies (105 pts.)	-1.01 (-0.63, 2.67)	374 fewer (807 fewer to 97 more)	⊕⊕⊖⊖ Low[a,b]
SG	RYGB	5 studies (721 pts.)	0.14 (-0.73, 0.99)	35 fewer (365 fewer to 105 more)	⊕⊕⊖⊖ Low[a,b]
D-RYGB	RYGB	1 study (123 pts.)	-0.04 (-2.02, 1.92)	9 more (701 fewer to 145 more)	⊕⊕⊖⊖ Low[a,b]
BPD-DS	RYGB	1 study (60 pts.)	-1.61 (-3.62, 0.39)	141 more (114 fewer to 150 more)	⊕⊕⊖⊖ Low[a,b]
BPD	RYGB	1 study (40 pts.)	-0.31 (-2.4, 1.8)	59 more (672 fewer to 148 more)	⊕⊕⊖⊖ Low[c]
B-RYGB	RYGB	1 study (60 pts.)	0.01 (-2.17, 2.22)	2 fewer (758 fewer to 147 more)	⊕⊕⊖⊖ Low[a,b]

[†] GRADE Working Group grades of evidence

High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different[‡] is low.

Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different[‡] is moderate.

Low = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different[‡] is high.

Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different[‡] is very high.

[§] Based on an assumption that 95% of patients who receive RYGB achieve significant weight reductions (TBWL>20%) after five years

[‡] Substantially different = a large enough difference that it might affect a decision

NMANMA-SOF-table definuition: ** Network metanalyses (NMA)reported as standardised mean differences (SMD), CrI: credible interval. Results are expressed in credible intervals as opposed to the confidence interval (CI) since a Bayesian analysis has been conducted.

Abbreviations: AGB: Adjustable gastric banding; BPD: Biliopancreatic diversion; BPD-DS: Biliopancreatic diversion with Duodenal Switch; B-RYGB: Banded RYGB; B-SG: Banded Sleeve Gastrectomy; D-RYGB: distal Roux-en-Y Gastric Bypass; OAGB: One Anastomosis Gastric Banding; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve gastrectomy

Explanatory footnotes:

[a] Downgraded due to risk of bias limitations

[b] Downgraded due to imprecision.

[c] Downgraded twice due to imprecision

Table 4: Summary of findings table of obesity surgery – diabetes outcomes – 2 years follow-up

Estimates of effects, credible intervals, and certainty of the evidence for comparison of bariatric surgery procedures for treatment of obesity – 2 years follow-up

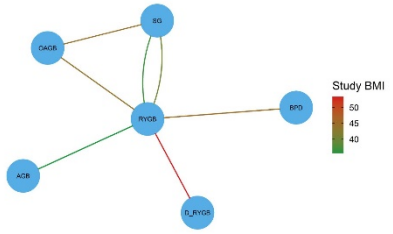
People: Adults with class II to III obesity, with or without comorbidity obesity

Settings: Bariatric clinics/hospitals

Intervention: AGB, SG, D-RYGB, OAGB, BPD

Comparator: RYGB (SG)

Outcome: diabetes control at 2 years follow-up



Intervention procedure	Comparator procedure	No of studies (no of pts.)	NMA estimate SMD (95%CrI)	Absolute effect[§††]	Quality of the evidence (GRADE)[†]
AGB	RYGB	1 study (46 pts.)	-0.34 (-1.3, 0.63)	135 more (276 fewer to 341 more)	⨁⨁◯◯ Low[a,b]
SG	RYGB	2 studies (149 pts.)	-0.13 (-0.41, 0.66)	55 more (188 fewer to 230 more)	⨁⨁◯◯ Low[a,b]
D-RYGB	RYGB	1 study (123 pts.)	-0.26 (-1.07, 0.54)	106 more (240 fewer to 313 more)	⨁⨁◯◯ Low[a,b]
OAGB	RYGB	1 study (253 pts.)	-0.58 (-1.2, 0.054)	211 more (18 fewer to 330 more)	⨁⨁◯◯ Low[a,b]
BPD	RYGB	1 study (40 pts.)	-1.32 (-2.12, -0.51)	343 more (191 more to 386 more)	⨁⨁◯◯ Low[c]
OAGB	SG	1 study (217 pts.)	-0.45 (-1.1, 0.17)	156 more (73 fewer too 278 more)	⨁⨁◯◯ Low[a,b]

[†] GRADE Working Group grades of evidence

High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different[‡] is low.

Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different[‡] is moderate.

Low = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different[‡] is high.

Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different[‡] is very high.

[§] Based on an assumption that 95% of patients who receive RYGB achieve significantly improved diabetes control at two years

[‡] Substantially different = a large enough difference that it might affect a decision

NMANMA-SOF-table definuition: ** Network metanalyses (NMA)reported as standardised mean differences (SMD), CrI: credible interval. Results are expressed in credible intervals as opposed to the confidence interval (CI) since a Bayesian analysis has been conducted.

Abbreviations: AGB: Adjustable gastric banding; BPD: Biliopancreatic diversion; BPD-DS: Biliopancreatic diversion with Duodenal Switch; B-RYGB: Banded RYGB; B-SG: Banded Sleeve Gastrectomy; D-RYGB: distal Roux-en-Y Gastric Bypass; OAGB: One Anastomosis Gastric Banding; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve gastrectomy

Explanatory footnotes:

[a] Downgraded due to risk of bias limitations

[b] Downgraded due to imprecision.

[c] Downgraded twice due to imprecision

Table 5: Summary of findings table of obesity surgery – diabetes outcomes – 3 years follow-up

Estimates of effects, credible intervals, and certainty of the evidence for comparison of bariatric surgery procedures for treatment of obesity

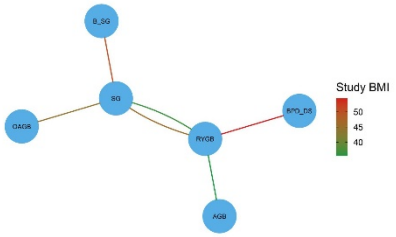
People: Adults with class II to III obesity, with or without comorbidity

Settings: Bariatric clinics/hospitals

Intervention: AGB, SG, OAGB, BPD-DS, B-SG

Comparator: RYGB (SG)

Outcome: diabetes control at 3 years follow-up



Intervention procedure	Comparator procedure	No of studies (no of pts.)	NMA estimate SMD (95%CrI)	Absolute effect[§]	Quality of the evidence (GRADE)[†]
AGB	RYGB	1 study (46 pts.)	0.27 (-0.62, 1.16)	122 fewer (431 fewer to 233 more)	⨁⨁⨀⨀ Low[a,b]
SG	RYGB	2 studies (340 pts.)	0.1 (-0.48, 0.67)	45 fewer (288 fewer to 190 more)	⨁⨀⨀⨀ Very Low[a,b,c]
OAGB	RYGB	1 study (217 pts.)	-0.55 (-1.49, 0.35)	212 more (157 fewer to 382 more)	⨁⨁⨀⨀ Low[a,b]
BPD-DS	RYGB	1 study (47 pts.)	-0.51 (-1.39, 0.37)	200 more (166 fewer to 373 more)	⨁⨁⨀⨀ Low[a,b]
B-SG	RYGB	1 study (94 pts.)	0.1 (-1.16, 1.35)	45 fewer (467 fewer to 346 more)	⨁⨁⨀⨀ Low[a,b]
OAGB	SG	NA	NA	NA	NA
B-SG	SG	NA	NA	NA	NA

[†] GRADE Working Group grades of evidence

High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different[‡] is low.

Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different[‡] is moderate.

Low = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different[‡] is high.

Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different[‡] is very high.

[§] Based on an assumption that 95% of patients who receive RYGB achieve significantly improved diabetes control after three years.

[‡] Substantially different = a large enough difference that it might affect a decision

bNMA-SOF-table definuition: ** Network metanalyses (NMA) reported as standardised mean differences (SMD), CrI: credible interval. Results are expressed in credible intervals as opposed to the confidence interval (CI) since a Bayesian analysis has been conducted.

Abbreviations: AGB: Adjustable gastric banding; BPD: Biliopancreatic diversion; BPD-DS: Biliopancreatic diversion with Duodenal Switch; B-RYGB: Banded RYGB; B-SG: Banded Sleeve Gastrectomy; D-RYGB: distal Roux-en-Y Gastric Bypass; OAGB: One Anastomosis Gastric Banding; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve gastrectomy

Explanatory footnotes:

[a] Downgraded due to risk of bias limitations

[b] Downgraded due to imprecision.

[c] Downgraded due to inconsistency

Table 6: Summary of findings table of obesity surgery – diabetes outcomes – 5 years follow-up

Estimates of effects, credible intervals, and certainty of the evidence for comparison of bariatric surgery procedures for treatment of obesity

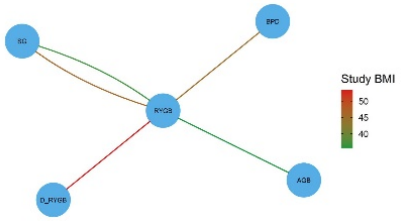
People: Adults with obesity class II or III, with or without comorbidity

Settings: Bariatric clinics/hospitals

Intervention: AGB, SG, BPD-DS, B-SG

Comparator: RYGB

Outcome: diabetes control at 5 years follow-up



Intervention procedure	Comparator procedure	No of studies (no of pts.)	NMA estimate SMD (95%CrI)	Absolute effect[§]	Quality of the evidence (GRADE)[†]
AGB	RYGB	1 study (46 pts.)	0.34 (-0.56, 1.25)	149 fewer (406 fewer to 234 more)	⨁⨁⨀⨀ Low[a,b]
SG	RYGB	2 studies (340 pts.)	0.13 (-0,47, 0.77)	59 fewer (302 fewer to 201 more)	⨁⨁⨀⨀ Low[a,b]
D-RYGB	RYGB	1 study (123 pts.)	-0.31 (-1.07, 0.46)	137 more (197 fewer to 378 more)	⨁⨁⨀⨀ Low[a,b]
BPD	RYGB	1 study (47 pts.)	-0.66 (-1.42, 0.1)	268 more (45 fewer to 429 more)	⨁⨁⨀⨀ Low[a,b]

[†] GRADE Working Group grades of evidence

High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different[‡] is low.

Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different[‡] is moderate.

Low = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different[‡] is high.

Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different[‡] is very high.

[§] Based on an assumption that 95% of patients who receive RYGB achieve significantly improved diabetes control after five years.

[‡] Substantially different = a large enough difference that it might affect a decision

NMANMA-SOF-table definuition: ** Network metanalyses (NMA)reported as standardised mean differences (SMD), CrI: credible interval. Results are expressed in credible intervals as opposed to the confidence interval (CI) since a Bayesian analysis has been conducted.

Abbreviations: AGB: Adjustable gastric banding; BPD: Biliopancreatic diversion; BPD-DS: Biliopancreatic diversion with Duodenal Switch; B-RYGB: Banded RYGB; B-SG: Banded Sleeve Gastrectomy; D-RYGB: distal Roux-en-Y Gastric Bypass; OAGB: One Anastomosis Gastric Banding; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve gastrectomy

Explanatory footnotes:

[a] Downgraded du to risk of bias limitations

[b] Downgraded due to imprecision

Table 7: Summary of findings table of obesity surgery – Early deaths <30 days after obesity surgery

People: adult people with obesity, with or without comorbidity
Settings: bariatric clinics/hospitals
Intervention: BPD-DS, RYGB, SR-RYGB
Comparison: head-to-head

Outcomes	Impacts	Expected no of deaths per 1000 people (95% CI)	Number of Studies	Certainty of the evidence (GRADE)*
BPD-DS				
Early deaths (<30 d after surgery)	1/53 (0.98%)	19 (1 to 101)	**2**	⨁⨁◯◯ **Low**[a,b]
RYGB				
	2/1,382 (0.14%)	2 (1 to 6)	**22**	⨁⨁◯◯ **Low**[b,c]
B-RYGB				
	1/230 people (0.5%)	4 (1 to 24)	**2**	⨁◯◯◯ **Very Low**[a,b,c]

Explanatory footnotes: downgraded due to the following reasons:

[a] Downgraded due to imprecision (few studies and wide CI),

[b] Downgraded due to high risk of bias;

[c] Downgraded due to potential risk of publication bias

BPD-DS: Biliopancreatic Diversion with Duodenal Switch; CI: Confidence Interval; RYGB: Roux-en-Y Gastric Bypass; B-RYGB: Silicon Ring RYGB

* GRADE Working Group grades of evidence High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different[†] is low. Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different is moderate. Low = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different is high. Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different is very high.

Table 8: Summary of findings table of obesity surgery – health-related quality of life (HRQOL) after obesity surgery

People: adult people with obesity, with or without comorbidities
Settings: Europe (8 studies); USA (1); Brazil (1), China (1)
Intervention: RYGB, SG, OAGB, BPD-DS, SR-RYGB, D-RYGB; B-SG (6 comparisons)
Comparison: head-to-head comparisons

Outcomes	Impacts	Number of studies	Certainty of the evidence (GRADE)*
HRQOL	All studies reported increased quality of life after surgery, with little to no differences in HRQOL between procedures.	**11**	⨁⨁◯◯ **Low**[a,b,c]

Explanatory footnotes: downgraded due to the following reasons:

[a] Downgraded due to high risk of bias in a majority of studies.

[b] Downgraded due to imprecision as few studies provided data for each comparison (and different tools were used)

[c] Downgraded due to potential risk of publication bias

BPD-DS: Biliopancreatic Diversion with Duodenal Switch; B-SG: Banded SG; D-RYGB: Distal RYGB; OAGB: One Anastomosis Gastric Bypass; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve gastrectomy

* GRADE Working Group grades of evidence. High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different[†] is low. Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different is moderate. Low = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different is high. Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different is very high.

Discussion

We were not able to identify treatments that consistently showed superior efficacy on weight loss or diabetes status in the NMA. Individual treatments indicated better outcomes in specific analyses. However, these differences were likely caused by heterogeneity and lack of transitivity. Our review includes up-to-date evidence from studies with longer follow-up than other recent SRs with NMAs.

We could not determine if hospital volume, the experience of surgeons, the type of setting (private/ community), or the type of procedure played a role in mortality after BS. A review including RCTs with small sample sizes and relatively short follow-up may not be the optimal study design for assessing short- or long-term mortality after bariatric surgery. Larger cohort studies with longer follow-up, or bariatric surgery registers, may be better suited to determine mortality after BS.

HRQOL was improved after surgery, independently of type of surgery, and with little or no difference between procedures. However, results for HRQOL were reported in less than half of the included studies, using a number of different instruments and reported in a way that did not allow for a quantitative analysis. We identified four ongoing studies focusing on quality-of-life outcomes for the comparison RYGB vs SG, one study comparing RYGB with vs AGB and one study with OAGB, which may help to explore potential differences between procedures further.

Assessing the risk of weight regain and of insufficient weight loss after BS turned out to be a challenge, with few studies reporting these outcomes, and various definitions used across studies, why the pooled results suggesting increased risk of conversion due to insufficient weight loss for AGB as compared to RYGB should be interpreted with caution.

Less than half of the included studies reported on CVD risk reduction, with mostly little differences between procedures (with the exception of BPD-DS, and D-RYGB showing improved lipid status). Since data on lipids, hypertension, and blood glucose are routinely collected at follow-up, there should be nothing preventing these important outcomes from being included in studies evaluating the effects of BS. Even fewer studies reported on micronutrient deficiencies, related metabolic complications and morbidity, and among these, the BPD-DS, D-RYGB and OAGB procedures were at potentially higher risk than RYGB, which is no surprise due to their malabsorptive nature. Also here caution must be in place when interpreting the un-pooled results of these single studies.

Our results suggest increased risk of GERD, and severe GERD requiring conversion surgery, as well as poorer resolution of GERD, in people with SG as compared to RYGB. A problem with this subjective outcome is ascertaining exactly what constitutes worsening GERD, or de novo GERD, since this was typically not well-defined in the included studies. In general, there was a lack of standardised classification and reporting especially of adverse events. Furthermore, there was great variation in comorbidities across included studies makes evaluations and interpretations of findings challenging.

The selection of only RCTs is another potential limitation, and it may be argued that well-performed cohort studies with longer follow-up could have provided valuable evidence for our research questions. However, allocation of participants to groups in non-randomised studies is typically based on patient preference, clinical decision-making, and shared clinical decison-making. Therefore, results from non-randomised studies may be biased because the characteristics of populations selected for a particular procedure may differ, limiting the usefulness of this evidence, in particular in the evaluation of head-to-head comparisons.

Conclusion

The results of this assessment suggest little or no difference in the effects of different bariatric surgery procedures (AGB, SG, RYGB, D-RYGB, OAGB, BPD-DS, and BPD) on weight loss and diabetes control. However, our results are based mainly on low to very low certainty evidence, with few or even single studies providing data for many of the comparisons. No evidence was found for the effectiveness of the more recent SADI-S or SASI procedures. No study reported on patient satisfaction with the procedure.

Improved HRQOL was consistently reported after bariatric surgery, but with little to no difference between procedures. We were unable to determine the relative effect of the different procedures on short- and long-term mortality, progression of obesity, and obesity-related co-morbidities. For most comparisons there was typically little to no difference in the effect on cardiovascular risk. Evidence from a couple of studies indicated beneficial effects of some of the more malabsorptive procedures (BPD-DS, BPD and D-RYGB) on cardiovascular risk reduction but entailing a potentially greater risk for micronutrient deficiencies and metabolic complications. There was some evidence suggesting greater problems with insufficient weight loss and re-operations in AGB, as compared to RYGB, and a greater risk of problems with GERD in patients with SG, including a greater risk of severe GERD that required conversion surgery, as compared to RYGB.

More high-quality research is needed to determine the relative effect of most obesity surgery procedures, as results for many comparisons are based on data from few studies at high risk of bias. There is also a need for studies with longer follow-up in order to assess the long-term effects of obesity surgery. The fact that most studies do not use the same classification for adverse events, and some other outcomes (e.g. weight regain, and insufficient weight loss) makes comparisons difficult. There is a need for standardised definitions, uniform classifications of adverse events, and reporting standards in this field of research to improve the evidence base.

1 SCOPE

The objective of this assessment was to determine the comparative effectiveness of surgical procedure for the treatment of obesity, for improving certain outcomes (e.g. weight, and diabetes control).

Description	Project scope
Population	Adults (≥18 y) with obesity, including the three groups described below [3] • Class 1: BMI ≥30 kg/m^2 and type 2 diabetes (T2D) who have not achieved durable improvement in glycaemic control with reasonable non-surgical methods [4] • Class 2: BMI ≥35 kg/m^2 and comorbidities (e.g. hypertension, diabetes) • Class 3: BMI ≥40 kg/m^2 Diagnosis CD-9-CM 278.00; Obesity, unspecified We did not include subgroups of patients of a certain age (e.g.>65 years), or people with a certain diagnosed disease, e.g. people with chronic kidney disease, or with heart failure only. Nor did we include studies of mixed groups including both patients who has received primary surgery and those undergone revisional (secondary) surgery, unless results for our group of interest were reported separately. MeSH-terms: *Morbid Obesities; Obesities, Morbid; Obesity, Severe; Obesities, Severe; Severe Obesities; Severe Obesity; Morbid Obesity* Intended use of the technology: treatment of obesity.
Intervention	1. Adjustable Gastric banding (AGB) 2. Sleeve gastrectomy (SG) 3. Roux-en-y gastric bypass (RYGB): 4. Distal Roux-en-y gastric bypass (D-RYGB) 5. Biliopancreatic diversion with duodenal switch (BPD-DS) 6. Biliopancreatic diversion (BPD) 7. One anastomosis gastric bypass (OAGB) In addition to the procedures listed above we included evidence on the effects of combined procedures (including banding or rings), BPD/DS, and of two new methods when available: • Single anastomosis duodenal-ileal bypass with sleeve gastrectomy (SADI-S) is a procedure based on the biliopancreatic diversion in which a sleeve gastrectomy is followed by an end-to-side duodeno-ileal diversion. • Single anastomosis sleeve ileal bypass (SASI) procedure is based on Santoro's operation, in which a sleeve gastrectomy is followed by a side-to-side gastro-ileal anastomosis. Bariatric surgery procedures are always combined with dietary/lifestyle interventions.
Comparison	Head-to-head comparisons across the different surgical procedures listed above, i.e. no comparison with routine medical care *Exclusions:* • Comparisons of surgical techniques/materials rather than of surgical procedures (e.g. robotic vs. non-robotic surgery, various types of sutures etc.) • Comparisons of open versus laparoscopic surgery (e.g. open Roux-en-y vs. laparoscopic Roux-en-y)

Description	Project scope

Comparison *(continuation)*	• Comparisons involving procedures that are no longer in use:
	  • Jejunoileal bypass
	  • Horizontal gastroplasty
	  • Vertical banded gastroplasty or vertical gastroplasty (not banded)
	  • Non-adjustable banded gastroplasty
	MeSH-terms: as per above

Outcomes	We will include the core outcomes identified as essential endpoints in all weight loss studies by the BARIACT study [5]
	Primary outcomes:
	• Measures of weight change (e.g.% excess weight loss, total weight loss, BMI reduction,% excess BMI reduction;% body fat loss)
	• Diabetes status:
	  ➢ *reduced need of antidiabetic agents (oral or injected) or reduction of the dosage – potential for substantial improvement in cost-effectiveness if patients on triple therapy with metformin +* gliflozins (*SGLT inhibitor)/ Glucagonlike Peptide (GLP analogue)/basal insulin can reduce to monotherapy following bariatric surgery*
	  ➢ *improved glycemic control (reduction in glycated hemoglobin (HbA1C) – so to consider the HbA1C as being on a continuum rather than a binary scale (controlled vs not-controlled)*
	• Health-related quality of life (HRQOL, assessed using a validated instrument)
	• Mortality (30-days and long-term)
	Secondary outcomes:
	• Cardiovascular risk reduction:
	  ➢ *Reversal of HbA1C: <6.0% without diabetic medication [6]*
	  ➢ *Resolution or improvement of dyslipidemia (e.g. achievement of Low Density Lipoprotein cholesterol (LDL)<2.59 mmol/L)*
	  ➢ *Reversal or improvement of hypertension (e.g. achievement of systolic Blood Pressure (BP)<140mmHG according to the American Diabetes Association standards (ADA)[7]*
	• Patient satisfaction with procedure
	• Adverse events**:**
	  ➢ *Technical complications of specific operation e.g. leaks, fistulas, strictures, and ulcerations at anastomosis, and gastric band problems*
	  ➢ *Any re-operation/re-intervention and classification of its severity*
	  ➢ *Dysphagia/regurgitation/gastroesophageal acid reflux disease (GERD)*
	  ➢ *Micronutrient status (i.e. total number of people with deficiencies in >1 micronutrient)*
	  ➢ *Post-operative morbidity including adverse events secondary to micronutrient deficiency (i.e. osteopenia and fractures)*
	• Resource use:
	  ➢ *Hospital length of stay (LOS) (if reported with primary outcomes)*
	  ➢ *Readmission to hospital (if reported with primary outcomes)*
	Due to limited resources in the project we will not consider the following AEs: cancer, kidney/renal, liver, pancreas, or thyroid function/disease, dental outcomes, or other rare consequences of micronutrient deficiencies (e.g. Beriberi, Wernicke's).

Description	Project scope
Study design	***Studies of effectiveness*** *Inclusion criteria* We included a relevant Cochrane Systematic review [8] on the topic, as it was suitable for our research question and complied with our PICO. We searched for and included RCTs published after the search date of this review (as described below). *Follow-up* We considered the following classification of follow-up after bariatric surgery as proposed by Mahawar in 2018 [9] • Short term: ≤1 year (≤12 months)* • Medium term: >1≤5 years (>12≤60 months) • Long term: >5≤10 years (>60≤120 months) • Very long term >10 years (>120 months) * This REA is limited to EFF studies with medium term and long term follow-up i.e. with >12 months follow-up after surgery. Studies with follow-up of 12 months or shorter were included in the SAF domain. ***Studies of safety*** *Inclusion criteria:* Health Technology Assessments (HTAs), Systematic reviews (SRs), and randomised controlled studies. We did not search for and included non-randomised controlled trials or observational studies, single arm trials and single or multiple arm prospective registry based data from national, regional, or hospital level registries. *Exclusion criteria* • Study designs other than those listed above, and with data collected from other sources than registries (e.g. through chart review, electronic health records, or patient surveys).
Language	Studies were considered eligible irrespective of language. However, all studies identified as eligible for inclusion were written in English.

2 METHODS AND EVIDENCE INCLUDED

2.1 Assessment Team

NIPHNO (author):

- Overall responsibility for production and quality of the assessment
- Recruited clinical experts, and attempted to recruit patient organizations
- Performed the scoping and literature search
- Collected the DOICUs from everyone involved in the assessment
- Developed the first draft of the project plan
- Carried out the assessment: selected and answered assessment elements (for the EFF and SAF domains)
- Quality-checked the production process for the TEC and CUR domains
- Sent draft versions to reviewers (dedicated reviewers, clinical experts) for comments, compiled feedback from reviewers and incorporated relevant changes to the draft
- Prepared all draft versions and the final assessment including an executive summary

HIQA (co-authors):

- Reviewed the project plan draft
- Filled in the checklist of potential “ethical, organizational, patient and social and legal aspects” of the HTA Core Model for rapid REA
- Selected and answered assessment elements for the TEC and CUR domains
- Approved/endorsed conclusions drawn

GÖG (co-authors):

- Provided assistance with data extraction.
- Provided feedback on draft report.

Dedicated reviewers (AQuAS, HAS, VASPVT):

- Reviewed the project plan draft, and the draft reports (including results and included studies).
- HAS- dedicated review of search strategy

The clinical experts supported the assessment team by:

- Discussing the project scope with the assessment team
- Reviewing the project plan
- Assisting in the selection of the most important AEs for decision-making
- Providing expert advice on the interpretation of study findings
- Reviewed the draft assessment

The statistician supported the assessment team by:

- Performing the NMA
- Providing text on NMA for the methods section, and the discussion.

2.2 Source of assessment elements

The published assessment protocol lists the assessment elements and the translated research questions that the assessment team agreed upon to evaluate. These elements are based on the assessment elements contained in the 'Model for Rapid Relative Effectiveness Assessment' (version 4.2) [10]. Additionally, assessment elements from other HTA Core Model Applications (for medical and surgical interventions, for diagnostic technologies or for screening) have been screened and included/merged with the existing questions if deemed relevant.

2.3 Search

We included RCTs only in both the EFF and the SAF domain. In a scoping search performed by an information specialist at NIPHNO, we identified a Cochrane systematic review from 2014 on the topic [8], which included 15 RCTs reporting head-on-head comparisons of different surgical procedures. The search in this review was from November 2013, and since their PICO was similar to the PICO in our assessment, we decided to limit our search to the period from 2013 up until the present.

The search strategy for this assessment was developed by information specialist Tonje Lehne Refsdal (TLR) at NIPHNO. After internal peer review of the search strategy by information specialist Gyri Hval (GH) at NIPHNO, and a EUnetHTA partner (Emmanuelle Blondet, HAS, France), the search strategy was finalised, and the searches were executed by TLR at NIPHNO.

The search strategy was based on the populations and interventions of the agreed PICOs. It contained both index terms and text words to identify as many relevant studies as possible.

As a first step, we searched for relevant systematic reviews and HTAs (Search I) to prevent unnecessary resource use and duplication of efforts. As a second step (Search II), we searched for primary studies (RCTs only). Reference list of relevant systematic reviews (and included studies) were searched to minimise the risk of missing relevant studies, which resulted in the identification of two additional records. In addition, we contacted manufacturers of bariatric rings and bandings about any published and unpublished (but not confidential) clinical studies providing evidence for their products. We had, if the time and resources allowed, planned to search also for non-randomised (safety) evidence, but this was not feasible due to the limited time available.

Appendix 1 includes the detailed search strategy.

Search I: Systematic Reviews and HTA

The searches were executed on 22 and 23 April 2020 with a year limit of 2013-2020
in the following databases:

- Cochrane Database of Systematic Reviews
- Embase (Ovid)
- Epistemonikos
- MEDLINE (Ovid)
- PROSPERO
- Web of Science

Search II: Primary studies

The searches were executed on 26 May 2020 with a year limit of 2013–2020 in the following databases:

- Cochrane Central Register of Controlled Trials
- Embase (Ovid)
- MEDLINE (Ovid)
- Web of Science

2.4 Study selection

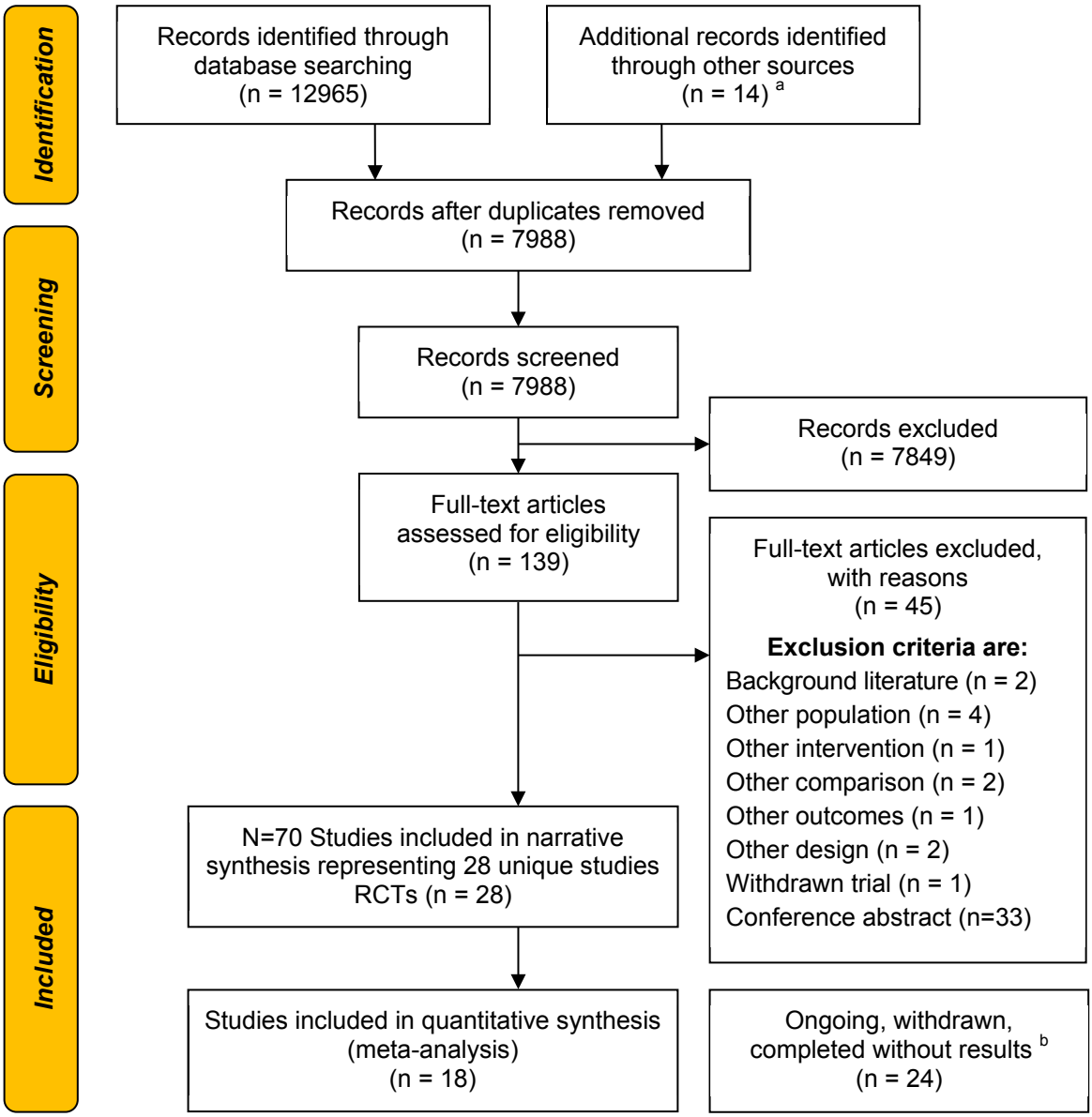


Figure 1: Flow chart

[a] Two additional studies identified through searching the reference lists of included studies and 12 studies identified in systematic review by Colquitt et al.

[b] Studies that are ongoing, withdrawn, completed without results identified through ClinicalTrials.gov, WHO ICTRP, and EU Clinical Trials Register searched through Cochrane Central Register of Controlled Trials, Issue 5 of 12, May 2020.

Two reviewers independently screened titles, abstracts and possibly relevant full texts according to PICOS criteria. Any disagreements in inclusion or exclusion of studies were resolved through discussion among review authors.

The search for existing evidence syntheses yielded 6,803 results and a search for primary studies yielded 6,162 results. After removal of duplicates, we ended up with 7,988 references. Two reviewers independently screened studies retrieved through the literature search against the predefined inclusion and exclusion criteria. After screening of titles and abstracts, we excluded 7,849 references. In the next step, we screened the remaining 139 studies in full text. Twenty-eight studies were included in this assessment, of which 22 were included in one or more quantitative analysis. The number of RCTs included in the NMA, treatments and patients for weight ranged between 11 studies, 8 treatments and 927 patients at 5 years follow-up, to 16 studies, 11 treatments and 2.288 patients at 2 years follow-up. The body of evidence for diabetes was considerably smaller and ranged from 5 RCTs, 5 treatments, and 455 patients at 5 years follow-up, to 6 studies, 6 treatments at 2 years follow-up and 666 patients at 3 years follow-up.

2.5 Data extraction and analyses

Data extraction and management

One reviewer (from GMF, SV, HS, and RP) used a piloted data extraction form to extract data from the included studies. A second author checked the accuracy of extracted data against the information in the included studies. Any disagreements were discussed and solved through discussion. The published project plan for this assessment lists the items that the assessment team agreed to extract.

In the case of missing, or unclear information in included studies, we contacted the authors (only once) for clarifications. Also, for trial protocols (i.e. terminated, unpublished or ongoing), we contacted the authors for further information when needed. Queries to study authors, investigators or sponsors may be necessary – details to be indicated in Appendix 4.

To characterise risk of early death, we used the available data to estimate risks and exact 95% binomial confidence intervals. We re-expressed estimates as expected numbers of early deaths per 1,000 people, rounding up to whole numbers of people. To compare treatments, we computed relative risks of early death and their 95% confidence intervals (we did not adjust for the multiple comparisons).

Traditional meta-analysis

We used traditional meta-analyses for assessing the comparative effectiveness of treatments on outcomes not included in the NMAs (i.e. risk of conversion surgery due to insufficient weight loss, or due to GERD). NMA was not an alternative, since typically less than 10 of the included studies provided data for the other outcomes. For these other analyses, we used Review Manager 5 (RevMan) [11]. Heterogeneity was quantified using the I 2 statistic [12]. For analyses with I2 >40% the random effect model was used [13], otherwise a fixed effect model was used. P-values less than 0.05, and CIs not including 1 were considered statistically significant for Risk Ratios (dichotomous outcomes).

Network meta-analysis (NMA)

We used network meta-analyses (NMA) in the Bayesian framework to pool the study results for diabetes and weight outcomes, two of our main outcomes. Because of the numerous bariatric procedures assessed in this REA, we determined it was feasible to use NMAs. All calculations were conducted within the R environment. The gemtc package version 0.8-8 was used to carry out the network meta-analyses [14]. The gemtc package relies on the rjags package [15]. The figures were created by a combination of several packages [16, 17]. We used the tidyverse package for data formatting [18].

Since the included studies reported a wide range of different weight and diabetes outcomes, we used standardised mean differences (SMD) as the basis for the NMAs. SMDs were calculated by the following formula:

$$SMD = \frac{Difference\ in\ mean\ outcomes\ between\ groups}{Standard\ deviation\ of\ the\ outcome\ between\ participants}$$

We used a ranked sequence of outcomes as the basis for the SMD. If a study reported multiple outcomes, we used the higher ranking outcome (for instance, we preferred BMI (kg/m^2) over Mean% excess weight loss) The ranking was created by a combination of clinical relevance (according to our clinical experts) and the frequency of included studies that reported this outcome (See Appendix 5) The ranking for weight-related outcomes was as follows:

1. BMI (kg/m^2) post intervention
2. Mean% excess weight loss (%EWL)
3. Mean change in BMI from BL
4. Weight (kg), post intervention
5. Mean weight change (kg) from BL
6. Mean% weight change from BL

The ranking for type 2 diabetes (T2D) outcomes was:

1. Mean HbA1c (%) post intervention
2. HbA1c% post intervention
3. Mean change in HbA1c (%) from BL
4. Mean% change in HbA1c from BL
5. Mean change in HbA1c (mmol/mol) from BL
6. Fasting plasma glucose (FPG) (mg/dL) or (mmol/L)
7. Mean change in FPG from BL
8. Mean% change in FPG from BL

If studies did not provide standard deviations (SD), we approximated it by using the confidence interval (CI) and the following formula in which N stands for the total number of study participants:

$$SD = \sqrt{N} \times \frac{(upper\ CI - lower\ CI)}{3{,}92}$$

In the event not enough data were available to approximate the SD for certain follow-ups, we used the baseline data or the mean SD of the other studies. One study did not report the sample size at 2 years follow-up [19]. Hence, we used the baseline sample size for this study.

We conducted NMA for 2, 3 and 5 years follow-up. Since the random effects models are known to produce overly conservative results in sparse networks [20], we also report the results of the fixed effect model. We used the vague default priors as provided by the gemtc package [14].

Since heterogeneity, transitivity (whether a comparison of two treatments via a third is appropriate) and consistency (the statistical manifestation of transitivity) are especially important in NMA, we took great care to assess the comparability of the included studies [21-23]. If the network architecture showed closed loops, we conducted an assessment of consistency with a node-splitting approach. The node-splitting method tests whether the direct and the indirect comparisons lead to similar effect estimates. If the estimates differ significantly, the results are judged as inconsistent. All tests for consistency require that indirect evidence can be compared with direct evidence (closed loops). Additionally, we analysed potential risks of transitivity by assessing study heterogeneity nonstatistically by reviewing the charcteristics of individual trials [12, 24, 25]. Finally, we used interactive network plots and visualised potential sources for heterogeneity (age, or BMI). If the network architecture showed closed loops, we conducted an assessment of consistency with a node-splitting approach.

Convergence was assessed graphically and statistically. For this purpose, we created density plots of the posterior effect estimate. If the plot deviated considerably from a normal distribution, we adjusted the model settings. Additionally, we used the Potential Scale Reduction Factor (PSRF) as the indicator for convergence. Values above 1.05 were considered dissatisfactory, and the calculations were repeated with adjusted model settings. The following settings were used for all calculations: 50,000 adaptations, 1,000,000 iterations and a thinning factor of 100.

The pooled results regarding treatment efficacy are summarised in figures. The surface under the cumulative ranking curve (SUCRA) permits ordering surgical treatments along their pooled efficacy. They show the probability of a treatment to rank a certain place or better. Since the sole presentation of SUCRAs can be misleading, we present them in combination with forest plots.

P values less than 0.05 and 95% CIs or 95% CrIs that did not include 0 were considered to be statistically significant (SMD weight and SMD diabetes status).

Estimation of number needed to treat

We estimated the number needed to treat for an additional beneficial or harmful outcome, with 95% CIs, by converting the SMDs comparing treatment to control to Odds ratios (ORs).

2.6 Quality rating

Two reviewers independently appraised the risk of bias (Table A26, Table A27, Figure A1) at study and outcome level using the Cochrane Risk of bias tool [1] with a couple of additional items from the Cochrane EPOC group [26]. Any disagreements were resolved by discussion between review authors. Studies were included discounting risk of bias. If an individual domain had a high/serious risk of bias, the overall judgement was that the study as a whole had a high risk of bias, irrespective of the domain at high risk. We used the grade tool to rate the certainty of the evidence for each primary outcome, taking into account the risk of bias, imprecision, inconsistency, indirectness and publication bias. Certainty of evidence/quality was judged as being high, moderate, low or very low as defined by the GRADE working group [2]. For the TEC and CUR domains, no quality tool was used. For the grading of the NMAs (weight and diabetes status), we followed the guidance in the Cochrane handbook [27]. We also used the RevMan software [11] to produce study level and outcome level risk of bias figures, to illustrate the risk of bias in included studies.

2.7 Patient involvement (if applicable)

We aimed to involve patients in this assessment but failed in our endeavours to engage with patients. We contacted both national (Landsforeningen for overvektige; or freely translated to English Norwegian Association for People with overweight) and international patient organisations (EASO ECPO – the European Coalition for People Living with Obesity). Both organisations were initially positive to participating/collaborating in the REA but in the end did not provide input. We also had an Open call for patient input (Jan-Feb 2020), which yielded no replies.

2.8 Description of the evidence used

Our protocol inclusion criteria for effect stated inclusion of RCTs only, and safety stated inclusion of RCTs only, if time and resources did not permit searching for and inclusion of non-randomised evidence. We did not have time and resources for a systematic search for non-randomised evidence. We included in total 28 unique studies, of which 6 reported only SAF outcomes, and/or had a follow-up of 12 months or shorter. Twenty-two studies reported EFF outcomes, of which 21 also reported SAF data. See Table 9. We followed up with trialists to find out if posters and abstracts had available results or full-text publication, see Appendix 4, Table A29. However, these contacts did not yield further evidence.

2.9 Deviations from project plan

In an intermediate stage of the production of this report, we changed the selection criteria to include combined procedures (i.e. B-RYGB and B-SG), and BPD/DS so as not to miss important data from the standard arm, and also because these procedures appear to be still in use in some countries. We had listed in the protocol both partial and complete resolution of diabetes as secondary outcomes of interest, but in the report we have focused on complete remission as this was the outcome reported in most studies, in addition to being a more robust outcome. We had planned to search for non-randomised studies addressing long-term effects of the different obesity surgery procedures, but due to lack of time and resources, this was not done. We had also planned to conduct subgroup analyses by obesity class, but because there were too few studies providing data for each comparison, subgroup analyses could not be executed.

Table 9: Main characteristics of studies included

Author and year or study name	Study type	Number of patients	Intervention (s)	Main endpoints	Included in clinical effectiveness and/or safety domain
Angrisani 2007 [28]; Angrisani 2013 [29]	RCT	51	RYGB; AGB	% EWL, BMI, weight, reoperations, complications, and comorbidities	EFF, SAF
Arceo-Olaiz 2008 [30]; Zarate 2013 [31]	RCT	60	RYGB; B-RYGB	%EWL, BMI, complications	EFF, SAF
Aasheim 2009 [32]; Søvik 2010 [33]; Søvik 2011[34]; Risstad 2015 [35]	RCT	60	RYGB; BPD-DS	BMI, anthropometric outcomes, HRQoL, complications/ AEs, CVD risk factors, lung function, vitamin status, and readmissions	EFF, SAF
Biter 2020 [19]	RCT	623	RYGB; SG	BMI	EFF
Capristo 2018 [36]	RCT	120	RYGB; SG	AEs	SAF
Courcoulas 2014, 2015 and 2020 [37-39] TRIABETES	RCT	69	RYGB; AGB	T2D remission, weight loss (kg),% weight loss, BMI, glycaemic control and medication, lipid profile changes, blood pressure, AEs	EFF, SAF
Fahmy 2018 [40]	RCT	60	RYGB; OAGB	AEs	SAF
Fink 2020 [41] MISO	RCT	94	SG; B-SG	%EWL	EFF, SAF
Hedberg 2012 [42]	RCT	47	RYGB; BPD-DS	EBMIL, weight change, HbA1c level, AEs (some outcomes were questionnaire assessed)	EFF, SAF
Helmiø 2012 [43]; Helmiø 2014 [44]; Salminen 2018 [45] SLEEVEPASS	RCT	240	RYGB; SG	%EWL, resolution of comorbidities, QOL, mortality, and early AEs	EFF, SAF
Himpens 2006 [46]	RCT	80	SG; AGB	Weight loss, GERD, complications and re-operations	EFF; SAF
Hofsø 2019 [47] OSEBERG	RCT	109	RYGB; SG	AEs	SAF
Ignat 2017 [48]: Vix 2013 [49]	RCT	100	RYGB; SG	EWL, QoL, co-morbidity, vitamin and glycolipid status, AEs	EFF, SAF
Karamanakos 2008 [50]; Kehagias 2011 [51]	RCT	32	RYGB; SG	%EWL, complications, improvement of obesity related comorbidities and nutritional deficiencies, AEs	EFF, SAF

Author and year or study name	Study type	Number of patients	Intervention (s)	Main endpoints	Included in clinical effectiveness and/or safety domain
Keidar 2013 [52]	RCT	41	RYGB; SG	AEs	SAF
Mingrone 2012, 2015 [53, 54] DIBASY	RCT	60	RYGB; BPD	Rate of diabetes remission	EFF; SAF
Murphy 2018 [55]	RCT	114	B-RYGB; SG	AEs	SAF
Nguyen 2009 [56]; Nguyen 2018 [57]	RCT	250	RYGB; AGB	Weight loss, BMI loss, morbidity, comorbidities, QOL LoS, mortality, reoperation rate	EFF; SAF
Paluszkiewicz 2012 [58]	RCT	72	RYGB (open); SG	Complications, mortality, reoperations, comorbidities and nutritional deficiencies	SAF
Peterli 2014 [59]; Peterli 2015 [60]; Peterli 2018 [61] SMBOSS	RCT	217	RYGB; SG	%BMIL, QoL, resolution of comorbidities, complications/AEs	EFF, SAF
Rasera 2015 [62]	RCT	400	RYGB; SR-RYGB	%EWL, QoL, and complications	EFF, SAF
Robert 2019 [63] YOMEGA	RCT	261	RYGB; OAGB	% EBMIL; AEs	EFF, SAF
Schauer 2012 [64]: Schauer 2014 [65]; Schauer 2017 [66] STAMPEDE	RCT	150	RYGB; SG	HbA1c≤ 6.0% with or without diabetes medication, weight and BMI reduction. AEs	EFF, SAF
Seethamaraiah 2017 [67]; Shivakumar 2018 [68]	RCT	201	SG; OAGB	%EWL, QoL, complications, 'resolution of comorbidities and AEs	EFF, SAF
Svanevik 2015 [35]; Risstad 2016 [69]; Svanevik 2018 [70]	RCT	113	RYGB; D-RYGB	BMI change, HRQoL, cardiometabolic risk factors, nutritional outcomes, AEs	EFF, SAF
Tognoni 2016 [71]; Gentileschi 2020 [72]	RCT	50	SG; B-SG	%EBMIL, complication rate, mortality and other AEs,	EFF, SAF
Wallenius 2020 [73] CONTROL	RCT	49	RYGB; SG	DM remission rate, BMI, waist circumference, glucose homeostasis	EFF, SAF
Zhang 2014 [74]	RCT	64	RYGB; SG	%EWL, BMI, QoL, morbidity rate, and resolution or improvement of comorbidities	EFF, SAF

Abbreviations: AE: Adverse Event; AGB: Adjustable Gastric Banding; BPD: Biiopancreatic diversion; BPD-DS: BileoPancreaticDiversion with Duodenal Switch; B-RYGB: Banded Roux-en-y Gastric Bypass; B-SG: Banded Sleeve Gastrectomy; DM: Diabetes Mellitus; D-RYGB: Distal Roux-en-y Gastric Bypass; DS: Duodenal switch; EFF: Effectiveness; EWL: Excess Weight Loss; HRQoL: Health Related Quality of Life; LoS: Length of Stay: OAGB: One anastomosis Gastric Bypass; QoL: Quality of Life; RCT: Randomised Controlled trial; RYGB: Roux-en-y Gastric Bypass; SAF: Safety; SG: Sleeve gastrectomy; SR-RYGB: Silicon-Ring Roux-en-y Gastric Bypass.

3 DESCRIPTION AND TECHNICAL CHARACTERISTICS OF TECHNOLOGY (TEC)

3.1 Research questions

Element ID	Research question
B0001	What is bariatric surgery?
B0002	What are the claimed benefits and potential risks associated with each type of bariatric surgery in current use?
B0003	What is the phase of development and implementation of bariatric surgery?
A0011	What is the current use and reimbursement status of the different bariatric procedures in Europe?
A0021	What is the reimbursement status of the technology?
B0004	Who performs bariatric surgery and in what context and level of care are they provided?
B0008 B0009	What kind of special premises, equipment and supplies are needed to perform bariatric surgery?
A0020	For which indications has the adjustable gastric band received marketing authorisation or CE marking?

3.2 Results

Features of the technology and comparators

[B0001] – What is Bariatric surgery?

Bariatric surgery (also known as obesity surgery, weight loss surgery or, in specific clinical circumstances, metabolic surgery) is the alteration of gastrointestinal anatomy and physiology using surgical methods with the aim of producing significant and sustained weight loss and resolution of, or improvement in, weight-related comorbidities, in particular type 2 diabetes (T2D). For the purposes of the assessment, the technology under consideration is any bariatric surgical procedure in current use for the treatment of obesity (defined according to the WHO criteria as a BMI ≥30 kg/m^2 in European populations) [75] and its associated complications. The comparator may be any other bariatric surgical procedure.

Bariatric surgical procedures cause a reduction in weight by reducing the volume of the stomach, causing malabsorption of nutrients, or by a combination of gastric restriction and malabsorption [76]. As well as the surgically-induced structural changes in the gastrointestinal tract, bariatric surgery changes the body's metabolism and hormonal responses resulting in physiological changes that can be used to manage certain chronic diseases that cannot be managed successfully using non-surgical methods [77].

Traditionally, bariatric surgical procedures have been divided into restrictive and malabsorptive procedures or a combination of both. Restrictive procedures include adjustable gastric banding (AGB), and sleeve gastrectomy (SG). The goal of such procedures is to produce early satiety and a consequent reduction in food intake by reducing the capacity or size of the stomach while maintaining the normal continuity of the gastrointestinal tract [78, 79]. Malabsorptive techniques bypass parts of the digestive tract and divert biliopancreatic secretions. Any procedure that dramatically

alters the structure of the gastrointestinal tract will affect the intake of nutrients [78]. Biliopancreatic diversion with duodenal switch (BPD-DS), Roux-en-Y gastric bypass (RYGB) and one anastomosis gastric bypass (OAGB) can be defined as combination procedures, having both restrictive and malabsorptive features. It is now recognised that this categorisation represents a substantial oversimplification of the mechanisms of action of bariatric surgical procedures. Beyond the extensive metabolic and anatomical changes that accompany bariatric surgery, inflammatory responses, changes in neural and endocrine signaling, gut microbial factors as well as learned behaviour change contribute to the overall benefits of surgery [78, 80]. Current guidelines refer to many of the bariatric surgical procedures as metabolic operations, where the primary indication for surgery is to achieve improvement in metabolic endpoints, reflecting the shift in the focus of bariatric surgery as primarily a weight-loss intervention to consideration of the metabolic effects of the operations [4]. In addition to the established procedures listed above, two combination procedures emerged recently, single anastomosis duodenal-ileal bypass with sleeve gastrectomy (SADI-S) and single anastomosis sleeve ileal bypass (SASI). Of note, bariatric/metabolic surgery is performed as part of a multicomponent lifestyle intervention including diet and physical activity, as detailed in [A0025].

The surgical procedures considered in this review are described below in order of increasing technical complexity, with similar procedures grouped together.

Adjustable gastric banding (AGB)

AGB is considered a fully reversible intervention that is typically performed laparoscopically (LAGB). The surgeon positions an inflatable ring or band around the uppermost part of the stomach, 1-2 cm below the gastro-oesophageal junction [78, 81]. When the band is inflated, it separates the stomach into two parts. The small upper gastric pouch above the band communicates with the rest of the stomach through a narrow channel created by the band. Less food is required to fill the uppermost portion of the stomach, limiting the amount of food that can be eaten [81]. The band is connected to a small device, called a port, placed under the skin [82]. The degree of constriction of the stomach can be adjusted by injecting or removing the saline solution through the subcutaneous port [78, 82]. LAGB is considered to be primarily a restrictive intervention and does not affect the absorption of nutrients [82, 83]. After surgery, several follow-up visits are required to adjust the tightness of the band to determine the optimal size of the opening between the gastric pouch and the rest of the stomach for the individual patient.

Mechanistic studies have suggested that the neurohormonal and metabolic changes demonstrated with bypass procedures or SG do not occur following insertion of an AGB, even following equivalent weight loss [84, 85]. While the surgery is less likely to result in nutritional problems, band-related failure or complications in the medium- to long-term (for example, band slippage/migration, erosion) necessitating revision surgery have led to a decline in the use of this procedure in some countries [85].

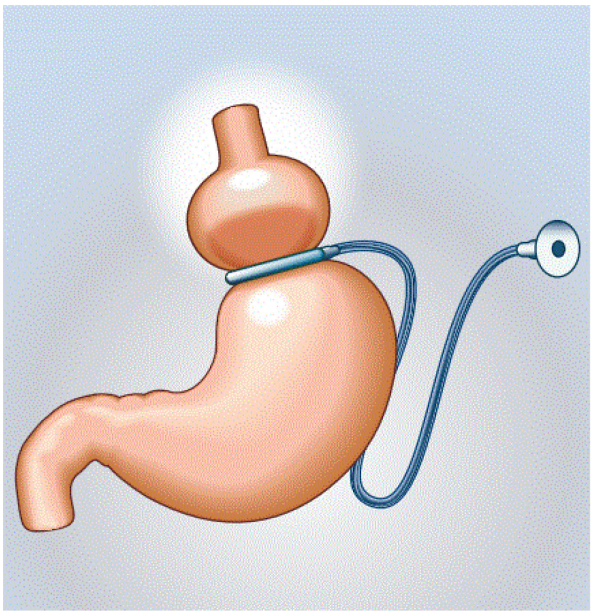


Figure 2:
Diagram depicting the AGB procedure with the adjustable band in place around the uppermost part of the stomach

Source: Haute Autorité de Santé (HAS): Technique de l'anneau gastrique ajustable. 2009.

Sleeve gastrectomy (SG)

With SG (also known as vertical sleeve gastrectomy or gastric sleeve surgery), most of the stomach is removed, with only a tube-shaped portion, or 'sleeve' remaining with a capacity of approximately 100-200 ml [86, 87]. This restricts the amount of food that the stomach can accommodate and accelerates gastric emptying [88]. Removing part of the stomach may also affect gut hormones (for example, ghrelin) or other factors such as the gut microbiome that may impact appetite and metabolism [81]. It is suggested that sleeve gastrectomy is an effective procedure that results in excellent weight loss and improvement of T2D [85]. It is also suggested that it may be a valuable option to treat T2D, especially in patients for whom there are concerns regarding the risk of post-operative complications associated with procedures that involve bowel diversion [85, 86].

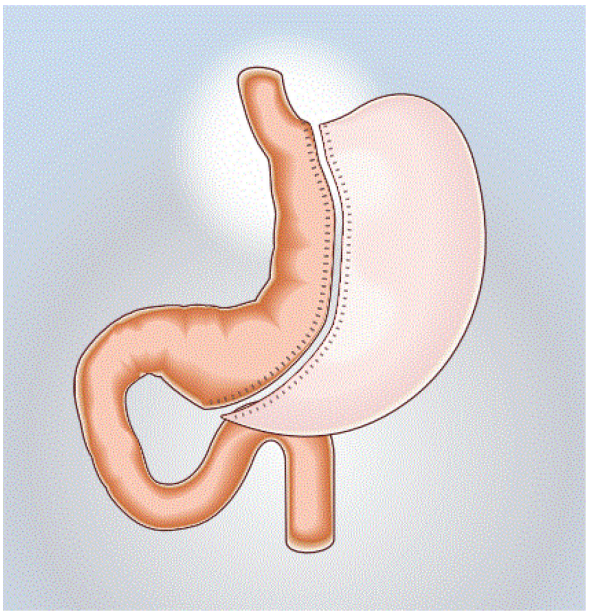


Figure 3:
Diagram depicting the SG procedure and the tube-shaped portion of the stomach that remains after the vertical resection

Source: Haute Autorité de Santé (HAS): Technique de la gastrectomie longitudinale (ou gastrectomie en manchon ou *sleeve gastrectomy*). 2009.

Roux-en-Y gastric bypass (RYGB),

With the RYGB (often abbreviated as 'gastricbypass'), the stomach is divided into two sections to create a small pouch with 15-30 mL capacity at the uppermost part of the stomach [78, 81]. The jejunum (that is, part of the small intestine), is transected approximately 50 cm distal to the ligament of Treitz, creating a proximal and distal end of jejunum. The gastric pouch is then directly anastomosed to the distal end of the jejunum creating an alimentary or 'Roux' limb of typically 100–150 cm [86]. Food enters this small pouch of stomach and then passes into the jejunum, thereby bypassing the majority of the stomach, the duodenum (the most proximal part of the small intestine) and some of the jejunum. Bowel continuity is restored by an entero-enteric anastomosis between the biliopancreatic limb (that is, excluded proximal end of the jejunum and the gastric remnant) and the Roux limb to allow some stomach acid and digestive enzymes to eventually mix with the food in order to facilitate digestion and minimise nutritional deficiencies. Thus, after completion of the standard RYGB, there is an alimentary limb of 100–150 cm, a biliopancreatic limb of 50–100 cm [89], and a common channel of variable length, typically 300–500 cm [88]. The surgery works by reducing the amount of food that can be consumed and decreasing nutrient absorption [86]. RYGB has been associated with specific complications, namely internal herniation, which may result in subsequent bowel ischemia as well as chronic abdominal pain [84].

Variable limb lengths (the alimentary limb, biliopancreatic limb, and common channel) have been used in an effort to achieve optimal outcomes. A systematic review by Mahawar et al. [89] concluded that a range of 100–200 cm for the combined length for the biliopancreatic and alimentary limbs gives optimum results with Roux-en-Y gastric bypass in most patients. However, the lack of standardisation across studies presents challenges for the interpretation and comparison of studies.

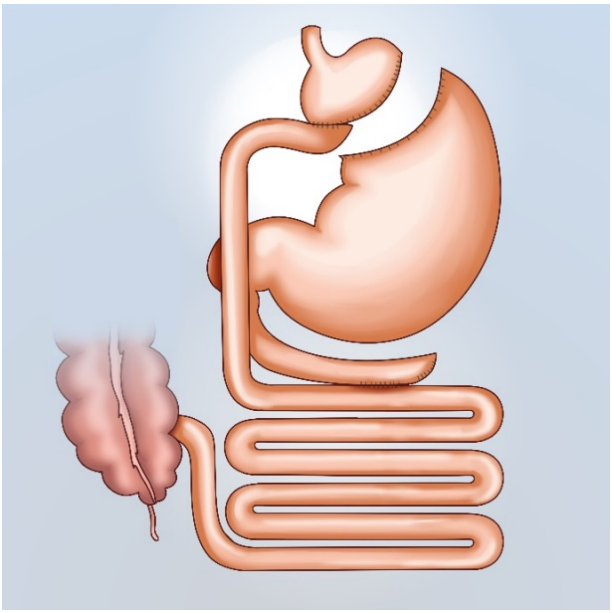


Figure 4:
Diagram depicting the standard RYGB procedure in which the stomach is divided to create a small gastric pouch which is then connected to the small intestine further down. The remnant gastric pouch and upper portion of the small intestine are reconnected to the small intestine

Illustration: Selma Flodgren.

Distal Roux-en-Y gastric bypass (D-RYGB)

Distal gastric bypass refers to a variant of gastric bypass where the distance from the small bowel anastomosis (entero-entero anastomosis) to the ileocecal valve is reduced [90]. Decreasing the length of the common channel reduces intestinal transit time and the surface area available for absorption, potentially leading to increased weight loss and greater improvements in comorbidities [91]. However, the risk of adverse nutritional deficiencies may be increased [90]. There is a delicate balance between greater weight loss and its associated health benefits achieved through modifications of the RYBG, along with a risk of surgical complications, such as nutritional deficiencies and dumping syndrome.

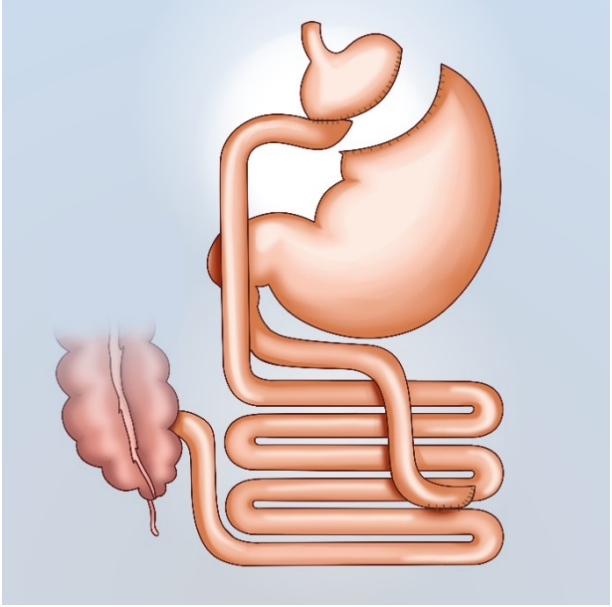


Figure 5:
Diagram depicting the D-RYGB procedure with the stump from the stomach bypassing a larger part of, and connecting to, a more distal part of the small intestines, than in standard RYGB

Illustration: Selma Flodgren.

One anastomosis gastric bypass (OAGB)

The OAGB (also known as the single anastomosis gastric bypass, mini-gastric bypass or omega-loop gastric by-pass) differs from the traditional RYGB which requires 2 anastomoses, but still combines both restrictive and malabsorptive mechanisms. During an OAGB procedure, the upper part of the stomach is divided into a tube. The tubular gastric pouch is then anastomosed to a loop of intestine, thereby bypassing up to 200 cm of the duodenum [92]. Patients undergoing OAGB are thought to be at a lower risk of anastomotic leak and perioperative complications in comparison to the RYGB, however long-term comparative data are lacking. Given the configuration of the anastomosis, there are concerns regarding bile reflux in to the gastric pouch with studies demonstrating a significant increase in postoperative rates of reflux, oesophagitis and nutritional deficiencies compared with RYGB [84].

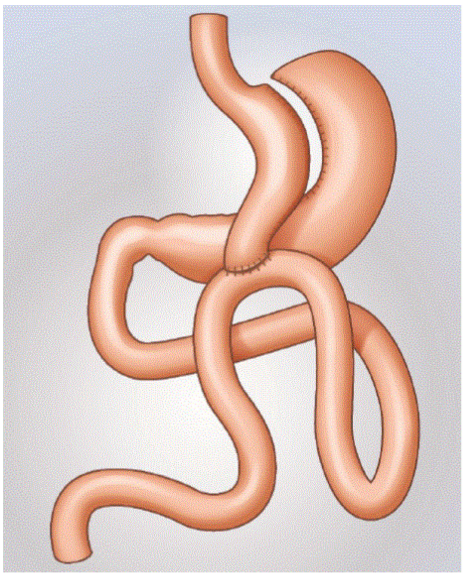


Figure 6:
Diagram depicting the OAGB procedure which combines one of the properties of SG and RYGB procedures. The upper part of the stomach is divided to form a tube, which is then joined to a loop of intestine further downstream

Source: Haute Autorité de Santé (HAS):
Surgical treatment of severe and massive obesity by one anastomosis gastric bypass. Technological Assessment report. 2019:13.

Biliopancreatic diversion (BPD)

Biliopancreatic diversion involves removing the lower portion of the stomach (distal gastrectomy) to form a gastric pouch. The remaining gastric pouch is then attached to the ileum (the final segment of the small intestine) bypassing a large portion of the small intestines [80, 93].

A modification of this procedure involving a duodenal switch, biliopancreatic diversion with duodenal switch (BPD-DS), which retains the pylorus, is now more commonly performed to minimise the risk of some complications including dumping syndrome, biliary reflux and marginal ulceration. The major difference between BPD and BPD-DS is that different parts of the stomach are removed during these procedures and the common limb length is longer in BPD-DS [80]. With BPD-DS, the pylorus is retained which reduces the risk of some complications.

Biliopancreatic diversion with duodenal switch (BPD-DS)

BPD-DS (sometimes abbreviated as duodenal switch) involves two separate components. The first part is similar to gastric sleeve surgery. A substantial proportion of the stomach is removed, leaving behind a smaller, tubular-shaped stomach pouch. The second part of the surgery is similar to the gastric bypass, except a larger portion of the small intestine is bypassed [76]. An incision is made in the duodenum (the first portion of the small intestine) just past the outlet of the stomach. The distal portion of the small intestine is then connected to the outlet of the tubular-shaped stomach pouch created in the first part of the surgery. Food passes through the newly created stomach pouch and empties directly into the last segment of the small intestine. Approximately 75% of the small intestine is bypassed during the surgery [76]. The bypassed portion of the small intestine contains bile and pancreatic enzymes necessary for the digestion and absorption of food. To facilitate digestion and adequate nutrient absorption, the bypassed section is reconnected to the last segment of the small intestine [76]. As food does not mix with bile and pancreatic enzymes until very far down the small intestine, the absorption of calories and nutrients (particularly protein and fat), as well as nutrients and vitamins dependent on fat for absorption (that is, fat soluble vitamins and nutrients), is significantly decreased [76]. The surgery also affects gut hormones in a manner that impacts hunger and satiety as well as blood sugar control [76]. While it is suggested that the BPD-DS is the most effective surgery in terms of weight loss and glycaemic control, it is also noted that it often leads to nutritional problems. Furthermore, the surgery is technically difficult to perform with an apparent increased risk of surgical complications [84, 85, 88].

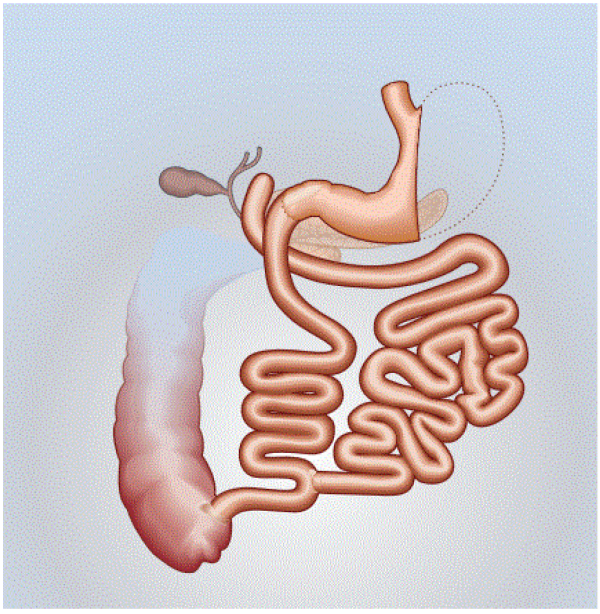


Figure 7:
Diagram depicting the BPD-DS procedure. with a smaller tube-shaped stomach being created through an SG, and bypassing a majority of the small intestines by connecting the end portion of the small intestine to the duodenum.the dotted line depicts the portion of the stomach that is removed during SG

Source: Haute Autorité de Santé (HAS): Technique de la dérivation biliopancréatique. 2009.

Single anastomosis duodenal-ileal bypass with sleeve gastrectomy (SADI-S)

SADI-S (also known as one anastomosis duodenal switch) was proposed as an alternative to the currently accepted BPD-DS procedure [94-96]. Initially, the size of the stomach is reduced through a sleeve gastrectomy. This leaves a tube of stomach passing from the oesophagus to the pylorus (that is, the opening from the stomach into the duodenum) and into the duodenum. The duodenum is then divided at the level of the gastroduodenal artery, leaving a short stump of duodenum attached to the pylorus. The distal end of the duodenum is closed off permanently. A loop of small bowel, usually 200 to 300 cm from the ileocaecal valve, is anastomosed to the short stump of duodenum arising from the pylorus to restore gut continuity [97].

For patients at high risk of complications from surgery, the procedure may be carried out in 2 stages: first sleeve gastrectomy, followed by duodenal transection and duodeno-ileal anastomosis in a subsequent procedure once the patient's surgical risks have been reduced as a result of weight loss induced by the initial sleeve gastrectomy [97].

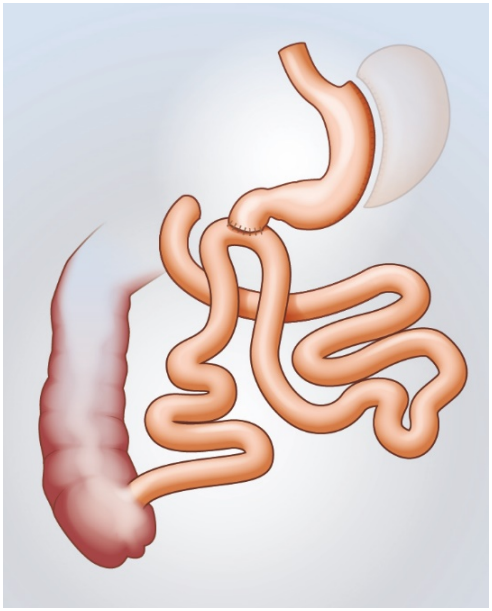


Figure 8:
Diagram depicting the SADI-S procedure which is a modification of the BPD-DS combining SG with RYGB, except with a single surgical anastomosis

Source: Haute Autorité de Santé (HAS):
Nouvelles techniques de chirugie bariatrique: identification, état d'avancement et opportunité d'évaluer. 2020.

Single anastomosis sleeve ileal (SASI) bypass

SASI bypass is a novel procedure in which a sleeve gastrectomy is followed by a single anastomosis between the reduced gastric pouch and the ileum (that is, the final part of the small intestine) [98]. This creates two potential routes for the transit of food; through the newly-created gastro-ileal anastomosis into the final part of the small intestine, and also through the duodenum as normal [99]. As the procedure does not exclude any part of the small intestine, the risk of nutritional deficiencies and malabsorption may be decreased relative to other malabsorptive procedures [99-102]. Reducing the number of intestinal anastomoses may be associated with shorter operative time and fewer anastomotic complications [101, 102].

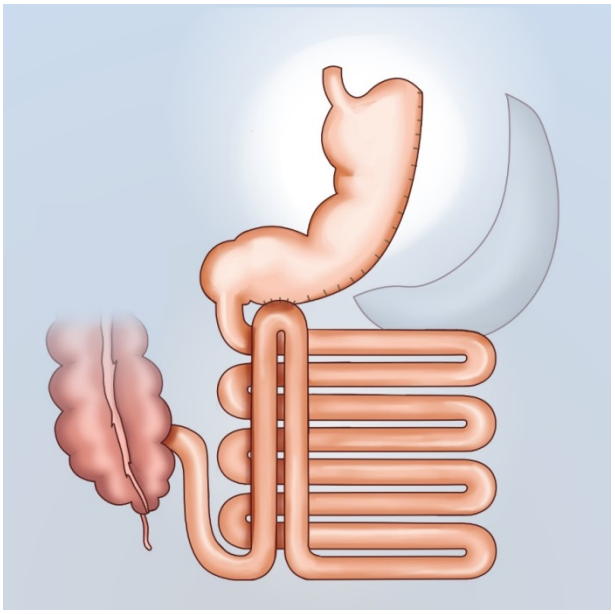


Figure 9:
Diagram depicting the SASI procedure with the distal part of the small intestine (approximately 3 meters before entering the colon) connecting directly to the stomach. The grey shape shows the resected part of the stomach

Illustration: Selma Flodgren.

Table 10: Summary of bariatric/metabolic surgery procedures in current use

	AGB	SG	RYGB	OAGB	BPD-DS	SADI-S	SASI
TECHNICAL ASPECTS							
International use	Less widely used in recent years	Widely used	Widely used	Not widely adopted; Increasingly used	Used in selected patients	Not widely adopted	Not widely adopted
Procedure*	Band placed around the upper part of the stomach (adjustable externally). Reversible.	Stomach restricted vertically to create a long narrow pouch. Irreversible.	Stomach reduced to a small pouch. Part of the stomach and small intestine bypassed. Requires two anastomoses. Irreversible (Can be revised to alter the length of bypassed intestines).	Alternative to RYBG. Gastric bypass procedure with a single anastomosis. Reversible and may be converted to RYGB [100].	Combination of sleeve gastrectomy and intestinal bypass. Requires two anastomoses. Partly reversible (Intestinal bypass is reversible; Sleeve gastrectomy is irreversible)	Simplified modification of BPD-DS. Sleeve gastrectomy followed by an end-to-side duodeno-ileal bypass. Single anastomosis. Partly reversible (Intestinal bypass is reversible; Sleeve gastrectomy is irreversible)	Sleeve gastrectomy is followed by a side-to-side gastro-ileal anastomosis. Partly reversible (Intestinal bypass is reversible; Sleeve gastrectomy is irreversible).
Mechanism of action	Restriction of food volume (variable depending on band tightness)	Restricts food volume. Changes in GI hormone secretion (e.g. ghrelin).	Restricts food volume. Reduces calorie and nutrient absorption. Changes in neuro-endocrine signalling.	Restricts food volume. Reduces calorie and nutrient absorption. Changes in neuro-endocrine signalling.	Restricts food volume. Greatly reduces calorie and nutrient absorption. Changes in neuro-endocrine signalling.	Restricts food volume. Reduces calorie and nutrient absorption. Changes in neuro-endocrine signalling.	Restricts food volume. Reduces calorie and nutrient absorption. Changes in neuro-endocrine signalling.
POTENTIAL PATIENT SELECTION CRITERIA							
Suitable candidates	The option to reverse the procedure is preferred [87, 103]. Patients without poorly controlled metabolic complications [87, 103].	Reference procedure. High-risk patients as a “first-stage” procedure. Not suitable for patients with severe GERD [4].	Reference procedure. Patients with GERD [4].	Not yet defined.	Severe/morbid obesity [103].	Unclear	Unclear

Key: BPD-DS – Biliopancreatic diversion with duodenal switch; GERD – gastro-intestinal reflux disease; GI – gastrointestinal; OAGB – One anastomosis gastric bypass; RYBG – Roux-en-Y Gastric Bypass; SADI-S – Single anastomosis duodenal-ileal bypass with sleeve gastrectomy (SADI-S); SASI – Single anastomosis sleeve ileal bypass; SG – sleeve gastrectomy; T2D – type 2 diabetes.

* Although reversal of intestinal bypass is possible it is considered a complex surgery with many associated risks.

Laparoscopic versus open surgery

Bariatric surgery can be performed through open or laparoscopic (also known as “keyhole” surgery or minimally invasive surgery) modalities [81]. According to the guidelines of the European Association for Endoscopic Surgery (EAES), laparoscopic surgery is now considered the gold standard approach for bariatric surgery, and should be undertaken in the absence of contra-indications [4].

According to the 2019 IFSO global registry report, which included data from 61 countries, 99.1% of procedures worldwide were carried out laparoscopically [104]. While the mode of surgery is different for laparoscopic and open bariatric procedures, the techniques used to perform the procedure remain the same. Laparoscopic surgery involves the use of an instrument called a “laparoscope” – a small tube with a light source and a camera, which relays images of the inside of the abdomen to an external monitor [105]. The benefits of laparoscopic surgery can include improved peri-operative outcomes (such as, shorter length of hospital stay, reduced blood loss and pain) compared with open procedures as well as faster post-operative recovery [105]. The approach chosen will depend on the individual case and the practices of the individual hospital or surgeon.

[B0002] – What are the claimed benefits and potential risks associated with each type of bariatric surgery in current use?

Weight-loss and improvements in obesity-associated comorbidities vary depending on the type of procedure as well as patient-derived risk factors [106]. At present, there is no single “gold standard” operation for bariatric/metabolic due to a lack of high-quality randomised controlled trials (RCTs) with long-term follow-up that provide head-to-head comparisons of different surgical procedures’ [4]. Guidance from the EAES published in 2020 promotes procedure-specific recommendations for the use of some well-established bariatric surgical procedures (RYGB and SG) [4]. However, specific recommendations to inform precise assignment of different procedures to individual patients for newer or investigational surgical procedures could not be issued due to the absence of long-term direct comparative evidence [4]. A better understanding of the risks and benefits associated with each type of bariatric/metabolic surgery, including an understanding of the exact mechanism of action of different surgical interventions, will contribute in the development of personalised treatment approaches. The clinical effectiveness of currently available bariatric/metabolic surgeries is described in the EFF and SAF domain.

Selection of the most appropriate procedure for an individual patient requires consideration of the clinical condition and medical history of the patient (including individualised goals of therapy: for example, weight loss and/or metabolic control), the risk-benefit ratio of the particular procedure and the expert judgement of the multi-disciplinary team (MDT).

In general, increased surgical manipulation of the gastrointestinal tract is associated with improved weight-related outcomes and metabolic endpoints (for example, improvement or remission of T2D) [85, 94]. However, there may be a greater risk of post-operative complications with increased surgical complexity and the associated increase in structural and functional changes to the gastrointestinal tract and neurohormonal changes in the gut-brain axis [94]. When assigning a patient to a specific bariatric/metabolic procedure the potential benefits of surgery need to be balanced against the risk of complications.

AGB

AGB is less technically challenging in comparison to the other types of bariatric surgery. The major benefits of this type of surgery include the relative operative rapidity, minimal invasiveness, the potential for reversibility and post-operative adjustability [107].

AGB can lead to satisfactory weight loss in selected patients, however a restrictive procedure may be unsuccessful if the patient follows a hypercaloric diet [108]. AGB tends to be recommended for patients with BMI of 30–40 kg/m^2 who have no significant co-morbidities, prefer a reversible procedure and will reliably engage with follow-up care [87, 103, 106].

SG

SG is a more complicated procedure than AGB because much of the stomach is removed. The intestinal tract remains unaltered, and so traditionally, SG is defined as a restrictive procedure, with fewer nutritional deficiencies expected because it is not a malabsorptive surgery [84]. However, in addition to restriction of food intake, the resection of the greater curvature of the stomach also alters gut hormones, in particular decreasing ghrelin production and resulting in suppression of hunger [109]. The beneficial effects of the surgery on glycaemic control have been suggested to derive from alterations in gastric motility and the resultant modified release of gastrointestinal hormones including glucagon-like peptide (GLP-1), peptide YY (PYY), and cholecystokinin (CCK) [87].

Technically, SG is considered an easier operation to carry out compared with malabsorptive procedures and is associated with a lower risk of nutritional deficiencies [84]. EAES guidelines have issued a conditional recommendation for the preferred use of SG over AGB for weight loss and control/resolution of metabolic comorbidities [4]. There is a rise in the use of SG internationally due to the lower risk of nutritional deficiencies associated with this type of surgery [104].

RYGB

RYGB procedures are technically more complicated than traditional restrictive procedures as they require remodelling of the anatomy of the gastrointestinal tract. Weight loss and metabolic improvements occur as a result of a reduction in food intake, intestinal malabsorption in addition to modifications in entero-endocrine signaling pathways (for example, increased PYY and GLP-1 levels) achieved through the alteration of the gastro-intestinal anatomy and physiology [87].

The surgery carries a higher risk of post-surgical complications when compared with restrictive procedures. Complications associated with RYGB include anastomotic leaks, anastomotic strictures, gastric remnant distension, marginal ulcers, internal hernia, early or late dumping syndrome (rapid gastric emptying), and micronutrient deficiencies [87]. EAES guidelines [4], DSS-II and 2013 AHA/ACC/TOS guidelines [106] all recommend the use of RYGB over AGB due to the evidence to suggest greater weight loss and control of T2D [4, 85, 106]. RYGB and SG are said to offer similar mid-term weight loss and control of metabolic complications [4].

In recent years, the use of RYGB has decreased in favour of SG [104]. However, RYGB is generally regarded as a procedure that produces long-term weight loss and resolution of obesity-related comorbidities with an acceptable risk profile and a considerable amount of long-term follow-up data to support its use [84, 110, 111]. There are certain indications which favour the use of this procedure, namely, the significant proportion of patients who suffer from GERD. EAES guidelines have issued a conditional recommendation for the preferred use of RYGB over SG in patients with severe GERD and/or severe esophagitis [4].

D-RYGB

Roux limb length has been shown to be correlated with weight loss in patients with BMI ≥50 kg/m^2 (super-obese) [112]. In D-RYGB, a modified form of RYGB, decreasing the length of the common channel could lead to greater weight loss and greater improvements in comorbidities compared to standard gastric bypass, however the risk of nutritional deficiencies may be increased [90].

A minimum length of approximately 100 cm for the common channel length has been suggested as essential to circumvent severe, adverse nutritional effects, although there is inter-individual variation in the risk of post-operative nutritional complications [90, 112, 113].

OAGB

The main advantage of the OAGB is its relative technical simplicity and reduced learning curve for surgeons in comparison to RYGB. The single anastomosis results in a shorter operating time and reduced operative risk by eliminating one anastomosis [95, 114].

Long-term, the procedure results in fewer intestinal obstruction problems and lower risk of internal herniation when compared to RYGB [114]. OAGB may offer greater short-term weight loss and resolution of T2D compared to RYGB, AGB and SG [4, 92]. However, there are some concerns in relation to nutritional deficiencies, biliary reflux, marginal ulcer, and esophago-gastric malignancy [114].

BPD-DS

The high incidence of post-gastrectomy syndrome associated with BPD led to modification of the procedure. In BPD-DS, pyloric preservation may reduce the risk of some complications including dumping syndrome, marginal ulceration and bile reflux when compared with BPD [93].

BPD-DS is the most technically challenging bariatric operation and, as such, may be associated with an increased risk of nutritional deficiencies in the long term including protein malnutrition, fat malabsorption and a number of micronutrient deficiencies [115].

BPD-DS can be performed in two separate stages to reduce peri-operative risk [87, 103]. The procedure has been associated with the most significant weight loss and improvements in metabolic disturbances of all bariatric surgical procedures [103, 108]. Despite the evidence to suggest that BPD-DS is the most effective surgery in terms of weight loss and glycaemic control, [4, 106] DSS-II recommendations suggest that BPD-DS should be considered only in patients with extreme levels of obesity (for example, BMI 60 kg/m^2) due to the risk of nutritional deficiencies [85].

Procedure selection

The choice of bariatric procedure is generally influenced by a number of factors including the best available evidence, specific local/regional conditions, the clinical experience of the available surgical multidisciplinary team (MDT), the individual patient's medical history including consideration of the individualised goals of treatment (for example, weight loss and/or metabolic control) [116, 117].

A major advantage of established bariatric surgery procedures (such as RYGB or AGB) is the availability of long-term data to support their use. Thus, risks can be monitored and managed appropriately. Longer-term data is needed prior to the introduction of newer procedures into routine use to inform appropriate patient selection. Despite the availability of long-term follow-up data for some procedures, it is typically not possible to accurately predict long-term weight-loss success or the risk of nutritional deficiencies. The differences in weight loss and glycaemic control is vast be-

tween but also within different bariatric operations, attributable in part to variation in the clinical condition of patients prior to surgery and adherence to post-surgical lifestyle changes among other factors [118, 119]. The choice of procedure requires rigorous consideration of the risk-benefit ratio. Safety, including the avoidance of possible postsurgical complications, remains the most important guiding factor for the choice of bariatric surgical procedure. An informed decision regarding the best procedure for an individual patient depends on the availability of long-term data, evidence from head-to-head comparative studies and reliable predictors of success or failure.

[B0004] – Who performs bariatric surgery and in what context and level of care are they provided?

Achieving good outcomes from bariatric surgery requires an optimal environment including multidisciplinary care by an experienced bariatric surgical team of health professionals, appropriate resources and equipment, a system for pre-operative patient assessment and ongoing monitoring during the post-operative period. Specific service standards for the provision of bariatric surgery have been developed by numerous professional societies and public health bodies including the Alberta Health Services [120], the British Obesity and Metabolic Surgery Society (BOMSS) [121, 122], the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) [123] the Spanish Ministry of Health Social Services and Equality and the Welsh Health Specialised Services Committee (WHSSC) [124]; however, no European-level guidance documents were identified.

Depending on the available resources, the complexity of the surgery and the clinical condition of the patient, bariatric surgery may be carried out in high-volume specialised centres with critical care facilities, or lower acuity hospitals where patients can be managed on the hospital ward [121-123].

Multidisciplinary team

The management of patients with obesity and its associated comorbidities undergoing bariatric surgery requires collaboration with multiple disciplines including nutrition, anaesthesiology, cardiology, pulmonary medicine, orthopaedic surgery, diabetology, psychiatry, and rehabilitation medicine. The MDT should have access to/include the most appropriate group of health care professionals required to make a comprehensive and appropriate decision for an individual patient [124]. BOMSS standards recommend that the specialist surgical MDT should, at a minimum, comprise bariatric surgeon(s), specialist dietician, bariatric specialist nurse and an experienced bariatric psychologist [121]. It is strongly recommended that either a bariatric physician, endocrinologist and/or an anaesthetist should be present at bariatric MDT meetings [121].

In addition to the core MDT described in BOMSS standards, MBSAQIP standards, WHSSC and National Health Service (NHS) service specifications advise that the core MDT is supported by a range of disciplines including physical or exercise therapy, physiotherapy, radiology and radiography, occupational therapy and social workers or other licenced behavioural health care providers during the preoperative, perioperative, and postoperative period [123-125]. Access to other specialties (for example, cardiology, pulmonology, and endocrinology) should be available where this is indicated [123]. Guidance from Spain indicates that in addition to the above, a plastic surgeon should be present on the MDT [122].

In the post-operative period, the frequency and type of care appointments (including monitoring for complications, medication review, nutritional and weight maintenance support) depends on the type of procedure, the patient's clinical needs and the presence of post-surgical complications [4, 124, 126, 127].

Volume criteria

Outcomes of surgery have been shown to be volume-dependent, with a general trend towards improved quality of care with higher surgical volumes [122-124]. Therefore, minimum volume requirements for institutions and surgeons may be necessary to reduce the risk of surgical complications through ongoing maintenance and improvement of professional competencies, as well as institutional structures and processes. European Accreditation Council for Bariatric Surgery (EAC-BS) [128], BOMSS [121] and MBSAQIP [123] report minimum volume requirements for surgeons and institutions; however, minimum volume thresholds are likely to be context-specific and should consider post-surgical morbidity and mortality data, the technical complexity of the particular surgery and the experience of the surgeon and MDT.

Level of care

The level of care required will depend on the level of need for critical care of an individual patient. The level of care required will range from high acute (for example, hospital ward) to critical care (for example, high dependency unit (level 2) or critical care unit (level 3)). According to 2019 MBSAQIP and 2019 BOMSS standards, the majority of patients can be safely cared for and closely observed/monitored with zero or single organ support in a level 1 surgical 'step down' unit for the first 24 hours post-surgery [121, 123]. For higher risk patients with potential or planned requirements for post-operative critical care, on-site critical care facilities should be available [121]. It is no longer considered mandatory for critical care (that is, level 2 or 3) facilities to be provided on-site, in circumstances where:

- patients are accurately risk-stratified pre-operatively to identify those who might require elective admission to critical care (including patients with severe and untreated sleep apnea (e.g. inability to tolerate CPAP)
- 24-hour consultant surgeon and anaesthetic cover is provided to support ward staff and junior doctors
- robust transfer arrangements are in place at every unit undertaking bariatric surgery for the safe transfer of patients requiring additional monitoring/support to critical care facilities (level 2 or 3, as appropriate) that have the capability to manage the full range of bariatric/metabolic surgery complications [121, 123].

[B0008] [B0009] – What kind of special premises, equipment and supplies are needed to perform bariatric surgery?

Bariatric surgery should only be undertaken in facilities that are adequately equipped to meet the needs of patients attending the service in order to ensure patient and staff safety. Healthcare settings carrying out bariatric surgery procedures should provide appropriate facilities and equipment for the care of metabolic and bariatric patients, including furniture, wheelchairs, operating room tables, appropriately weight-rated or reinforced toilets, beds, radiology capabilities, surgical instruments, and necessary facility requirements for the safe delivery of care to patients with obesity [123]. The EAC-BS has set out a number of institutional requirements in order to be recognised as a centre of excellence in bariatric and metabolic surgery [128]. Of note, bariatric surgery can be safely performed in non-specialist centres for appropriately risk-stratified patients.

In the context of this assessment, bariatric care needs refers to the considerations needed to provide safe and sensitive care throughout the care pathway (that is, during the pre-operative, peri-operative and post-operative period) for individuals with a larger body size for which standard size

hospital furniture, equipment, supplies and clinical procedures may not be appropriate, or with unique care needs related to obesity and its associated complications [120].

Key considerations for facilities managing patients with bariatric care needs include:

- equipment and furniture (for example, examination tables, wheelchairs) with appropriate weight capacity and dimensions to support and accommodate the patient
- appropriately sized supplies (for example, gowns, blood pressure cuffs, needles)
- the physical environment (for example, doorways, passageways, increased floor space) designed to accommodate patients with bariatric care needs
- all staff involved in the management of patients with bariatric care needs are trained and competent in the use of bariatric equipment [120].

Bariatric care needs assessment

Some patients with a diagnosis of obesity can safely use standardised furniture, equipment and supplies available in inpatient and outpatient settings if their weight is below the maximum weight capacity [120]. However, depending on individual's physical characteristics (for example, weight distribution, frame size, restricted access for tracheal intubation, reduced mobility), specialised equipment may still be necessary for patients below the maximum weight capacity of standard furniture and equipment [120]. Assessment of an individual patient's bariatric care needs during pre-surgical work-up will determine whether the procedure needs to be carried out in a centre specifically designed for the management of patients with morbid obesity with suitably modified equipment, or if care can be provided in lower acuity settings using standardised equipment [120].

Surgical theatre

For surgery performed laparoscopically, high definition video equipment with ergonomic positioning of monitors is necessary [129]. Appropriate instrumentation for laparoscopic and open bariatric surgery should be available at all times regardless of the chosen surgical approach for an individual patient, to enable emergency re-operation, or conversion to open surgery, if necessary [129].

Critical care facilities

In order to be recognised as a centre of excellence according to the EAC-BS centre of excellence programme, institutions must have critical care facilities on-site [128]. All facilities providing bariatric surgery services must be able to provide critical care facilities on-site or at another hospital capable of managing the full range of metabolic and bariatric surgery complications through an inter-hospital transfer agreement [121].

[A0020] – For which indications has the technology received marketing authorisation or CE marking?

The manufacturers of identified AGBs including, Allergan, Bariatric Solutions, Bariatec, Medtronic Covidien, Cousin Biotech, Helioscopie, Medical Innovation Development, Apollo Endo and Johnson and Johnson (Ethicon) were contacted to confirm the technical characteristics and regulatory status (Conformitè Europëenne (CE) marking) of these devices. However, only one manufacturer replied, Johnson and Johnson (Ethicon), who have discontinued production of the REALIZE® adjustable gastric band. Therefore, it is not possible to describe the indications for which identified AGBs are currently CE marked.

All gastric band system products including the associated calibration tube, access port and port needle, should carry the CE mark and should be compatible with the gastric band used. Table 11 details a list of adjustable gastric bands for which CE-marking and or FDA approval has been obtained. There is no centralised database of CE-marked products and their indications. In the absence of manufacturer feedback, details on regulatory status and indications for use are solely based on information retrieved from manufacturer websites.

Table 11: Indications for use and regulatory approval of adjustable gastric bands

Manufacturer	Technology	CE marking*	FDA approval*	Indicated use*
Bariatec Corporation [130]	GaBP Ring™	Unclear	Unclear	Unclear
ReShape Lifesciences, Inc.™ [131, 132]	LAP-BAND® Adjustable Gastric Banding System	Yes	Yes 2001	Adults with a BMI of ≥40 kg/m^2 or a BMI of ≥30 kg/m^2 with one or more obesity-related comorbid conditions who have failed more conservative weight reduction alternatives
Bariatric solutions [133, 134]	MiniMizer Extra gastric Band	Unclear	Unclear	Unclear
	MiniMizer gastric ring	Unclear	Unclear	Unclear
Cousin-Biotec [135]	Adjustable gastric band ADHESIX® BIORING®	Yes 2009	No	BMI ≥40 kg/m², or 35 to 40 kg/m² when combined with at least one comorbidity
	Adjustable gastric band BIORING®	Yes 2002	No	BMI ≥40 kg/m², or 35 to 40 kg/m² when combined with at least one comorbidity
Medical Innovation Development (MID) [136]	The MIDBAND™	Yes 2012	No	Adults with a BMI>40 (or 35 if combined with significant comorbidities likely to improve with the surgical intervention), who have been treated under suitable medical supervision and after a multidisciplinary evaluation
Agency for Medical Innovations (AMI) [137]	Soft Gastric Band Premium	Unclear	No	Unclear
Helioscopie [138-140]	HELIOGAST HAGA EV3 gastric band	Yes	No	Individuals with a BMI of >40 kg/m^2, or a BMI of 35-40 kg/m^2 with co-morbidities.
	HELIOGAST HAGE	Unclear	No	Individuals with a BMI of >40 kg/m^2, or a BMI of 35-40 kg/m^2 with co-morbidities.

*Based on the information reported on manufacturers websites.

[B0003] [A0021] [A0011] – What is the phase of development and implementation, current use and reimbursement status of the different bariatric procedures in Europe?

Indications for surgery

The majority of clinical guidelines in Europe recommend undertaking bariatric surgery in adults with a BMI ≥40 kg/m^2, or in adults with a BMI ≥35 kg/m^2 and at least 1 obesity-related comorbidity who have not achieved durable weight loss or improvement in comorbidities with optimal medical management (Figure 11).

There is strong agreement across clinical guidelines regarding the provision of bariatric surgery to patients with a BMI ≥35 kg/m^2, however, even in countries with a high level of bariatric surgical interventions, the provision of care is still below demand, particularly for patients with lower levels of obesity. In recent years, guidelines from professional societies including the American Diabetes

Association (ADA) [7], International Diabetes Federation (IDF) [141], and the International Federation for the Surgery of Obesity (IFSO) [94] have recommended adoption of a comorbidity-centric model for the selection of candidates for bariatric or metabolic surgery as opposed to traditional BMI-based eligibility criteria in order to facilitate prioritisation of access based on clinical need. However, these recommendations have not yet been adopted into clinical practice in all European countries. Guidance from England [127] Germany [142] and Belgium [83] have expanded indications to include patients with a BMI 30-34.9 kg/m^2 and recent-onset [127] or inadequately controlled T2D [83, 142]. In Norway [143]. Sweden [144], Denmark [145], Switzerland [146, 147], Spain [148, 149], France [150] and The Netherlands [151] traditional BMI criteria are also still in use (that is, BMI ≥35 kg/m^2 and obesity-related comorbidities or a BMI ≥40 kg/m^2).

In adults with a BMI above 50 kg/m^2, guidance in England, Germany and the Netherlands recommends that bariatric surgery should be considered as a first-line treatment [127, 142, 151], although guidance from the Swiss Society for the Study of Morbid Obesity and Metabolic Disorders (SMOB) recommends that patients with a BMI of ≥50 kg/m^2 should still attempt a reduced duration of conservative weight-loss management (that is, one year for patients with a BMI ≥50 kg/m^2 compared to 2 years for patients with a BMI <50 kg/m^2) prior to undergoing bariatric surgery [147].

Choice of procedure

In Europe, SG and RYGB are the most commonly performed surgical interventions for patients requiring weight loss and/or improved metabolic control. In general, BPD-DS and LABG are not widely used due to their less favourable risk-benefit profile. In particular, BPD-DS is typically only used in patients with severe obesity [83, 152]. In addition to the established procedures for which long-term data are available, several newer or alternative procedures are under investigation in ongoing clinical studies. According to the IFSO, OAGB is no longer regarded as new or experimental procedure and should be considered an acceptable mainstream surgical option [9]. However, long-term comparative data are still lacking [9]. Guidance from Canada published in 2020 has recommended against the use of this procedure due to the increased risk of complications in comparison with RYGB [153]. Assessments of new or alternative procedures (including OAGB, SADI-S and SASI) undertaken by HAS in 2019 and 2020 concluded that further clinical evidence is needed to determine the long-term efficacy and safety of these procedures prior to reimbursement by the French national health insurance scheme [96, 154]. In general, newer surgeries are not widely available in Europe due to the absence of long-term data [83, 95, 97, 147, 155]. The recommendations of national public health bodies in Europe are in accordance with the guidance set out by regional and international organisations and professional societies (Table A3).

Based on data from the Fifth IFSO Global Registry Report, the current use of bariatric surgical procedures in Europe is broadly in line with trends elsewhere [104]. Globally, between 2015 and 2018, SG was the most commonly performed procedure (58.6%), followed by RYGB (31.2%). There is a general trend towards a reduction in the rates of gastric banding and RYGB procedures being performed [104]. However, these trends may change pending the results of ongoing clinical studies of newer and alternative procedures. In particular, the uptake of OAGB appears to be significantly increasing [104].

Access to bariatric surgery and reimbursement

Access to bariatric surgery varies widely across Europe, and in general, there is insufficient capacity to meet demand in publicly funded health services, possibly attributable to poor continuity and coordination of care across multiple clinical care pathways [156]. According to the IFSO Global Registry Report 2019, the number of bariatric surgical procedures performed between 2015 and 2018 varied widely across Europe, despite similar rates of obesity, taking differences in the total

eligible population into account [104]. In Austria, Belgium, Bulgaria, Greece, Hungary, Ireland, Lithuania, Poland, Portugal, Switzerland, Turkey and the United Kingdom, on average, less than 10 procedures per 100,000 population per year were carried out during the period 2015 and 2018. On average, 13, 15 and 25 surgeries per 100,000 population per year were carried out in Italy and Norway, respectively, during the same period. In excess of 50 surgeries per 100,000 population were carried out in France, Iceland, The Netherlands and Sweden between 2015 and 2018. The 2019 IFSO global report highlights that the number of surgeries reported to be carried out in France is likely to be underestimated, possibly due to missing data. According to a national report, approximately 60,000 surgeries were carried out in France in 2016 corresponding to approximately 90 procedures per 100,000 of population [157]. Of the data reported in the IFSO Global Registry Report, it is unclear what proportion of the bariatric surgery operations were undertaken within publicly funded healthcare systems.

An analysis of bariatric surgery utilisation and funding across Europe reported that total spending on bariatric surgery ranged from €5 (Denmark) to €243 million (France), and represented per capita spending of between €0.54 (Germany) and €4.33 (Belgium) [158]. Obesity surgery is not reimbursed in Greece, Georgia and Slovakia [159].

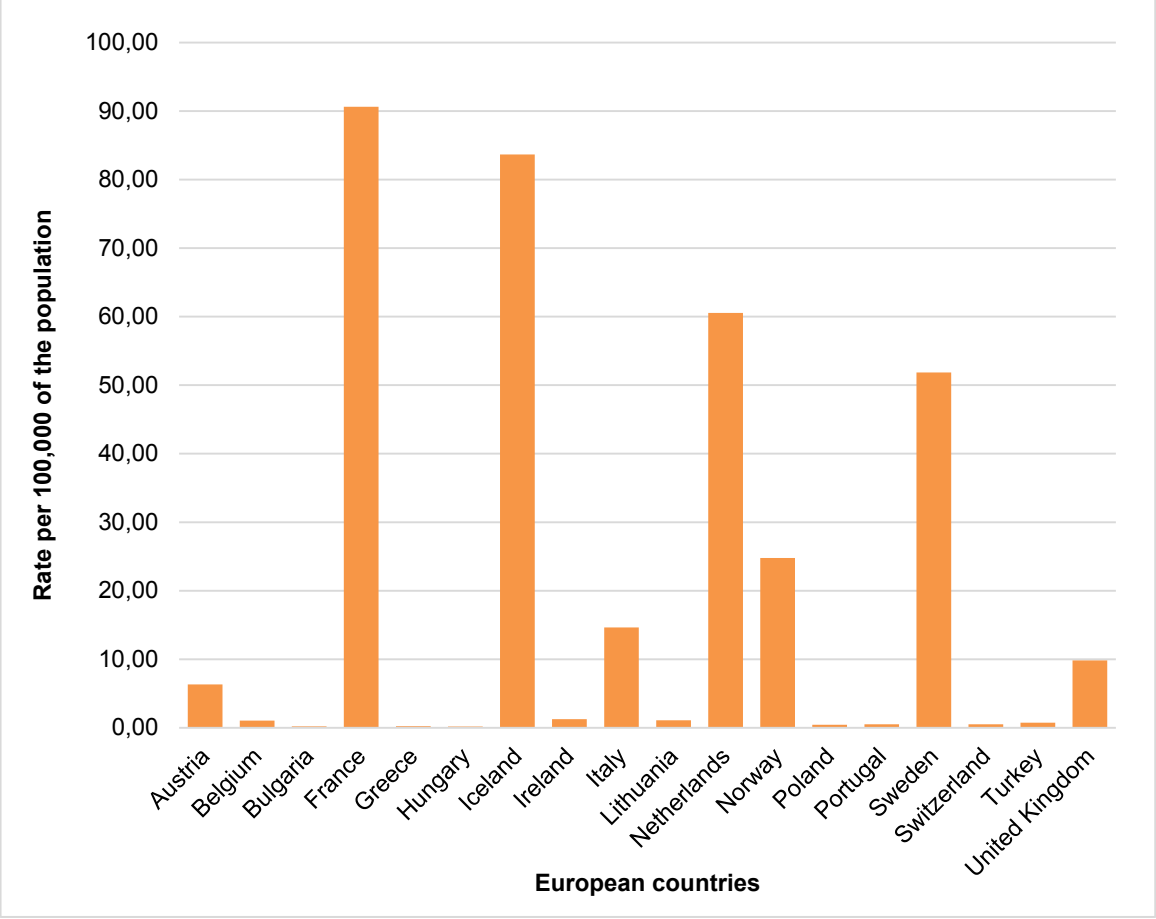


Figure 10: Number of surgical procedures per 100,000 of the population in selected European countries[*†]

* The absolute number of surgeries in European countries was identified from the 2019 IFSO global registry report, and expressed as the rate per 100,000 population based on population estimates available from the Organisation for Economic Co-operation and Development (OECD) [160].

† In some cases the absolute number of surgeries reported in the 2019 IFSO report may be underestimated. The level of bariatric surgical activity in France is based on a national report [157].

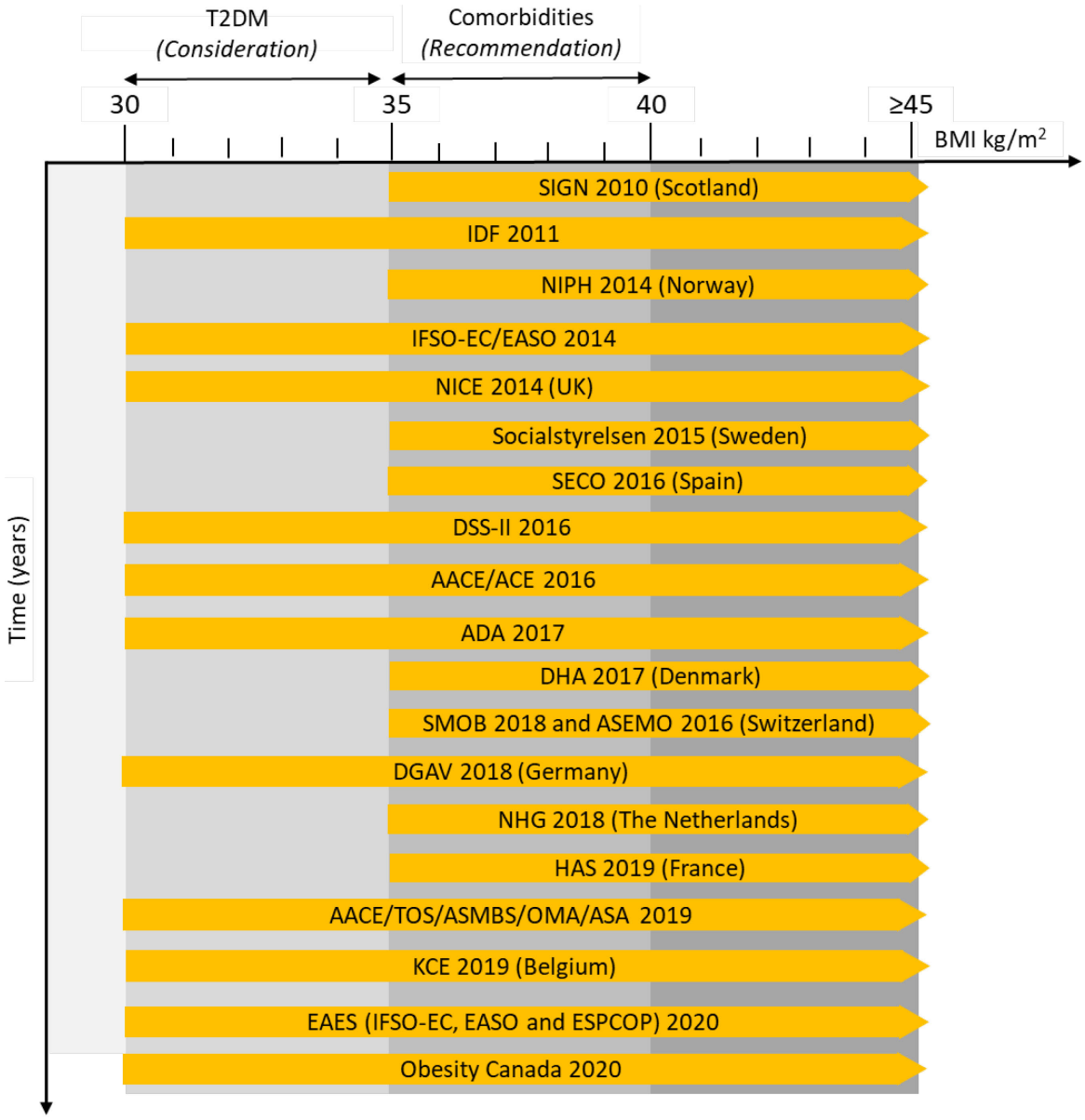


Figure 11: Minimum BMI and associated criteria for primary bariatric surgery in adults according to HTA agencies and professional societies

Key: AACE – American Association of Clinical Endocrinologists; ACE – American College of Endocrinology; ADA – American Diabetes Association; ASEMO – Swiss Association for the Study of Obesity; ASMBS – American Society for Metabolic and Bariatric Surgery; DGAV – German Society for General and Visceral Surgery; DHA – Danish Health Authority; DSS – Diabetes Surgery Summit; EAES – European Association of Endoscopic Surgery; EASO – European Association for the Study of Obesity; ESPCOP – European Society for the Peri-operative Care of the Obese Patient; FHI – the Swedish National Institute of Public Health; HAS – Haute Autorité de santé; IDF – International Diabetes Federation; IFSO-EC – European Chapter of the International Federation for the Surgery of Obesity and Metabolic Disorders; KCE – Belgian Health Care Knowledge Centre; NHG – The Dutch College of General Practioners; NICE – National Institute for Health and Care Excellence; NIPH – Norwegian Institute of Public Health; OMA – Obesity Medicine Association; SECO – Spanish Society for Obesity Surgery; SIGN – Scottish Intercollegiate Guidelines Network; SMOB – Swiss Society for the Study of Morbid Obesity and Metabolic Disorders; TOS – The Obesity Society.

* Refractory hypertension listed as an eligibility criterion in patients with class I obesity in EAES 2020 guidelines only.

Recommendations of each agency or society available in Appendix 1, Table A3.

4 HEALTH PROBLEM AND CURRENT USE OF THE TECHNOLOGY (CUR)

4.1 Research questions

Element ID	Research question
A0002	What is obesity?
A0007	What is the target population in this assessment?
A0023	How many people belong to the target population?
A0003	What are the known risk factors for obesity?
A0004	What is the natural course of obesity?
A0005	What are the symptoms and the burden of obesity for the patient?
A0006	What are the consequences of obesity for the society (prevalence, incidence, costs)?
A0024	How is obesity currently diagnosed according to published guidelines and in practice?
A0025	How is obesity currently managed according to published guidelines and in practice?
A0011	How much are the technologies utilised?“

4.2 Results

Overview of the disease or health condition

[A0002] – What is obesity?

Obesity is a chronic, complex, progressive disease characterised by excessive body fat accumulation that can result in multiple organ-specific consequences resulting in adverse metabolic, biomechanical and psychosocial consequences [161-166]. For most individuals with obesity, the aetiology of the disease is said to be influenced by multiple factors including obesogenic environments, psychosocial factors and genetic variants. In a subgroup of patients, single major aetiological factors can be identified such as genetic variants [166].

There are a number of ways to quantitatively define and categorise obesity. Anthropometric measurements such as BMI and waist circumference are typically used in clinical practice to detect obesity. BMI is the most widely used proxy for body fat to assess population-level rates of overweight and obesity, as it is easily calculated using a person’s weight and height. For adults, BMI is interpreted using standard weight categories, regardless of sex or age, although cut-offs can carry based on ethnicity [167]. The World Health Organization (WHO) defines BMI categories for overweight and obesity of 25-29.9 kg/m^2 and ≥30 kg/m^2, respectively (based on Caucasians with a Western lifestyle) [168]. A detailed description of available methods to estimate body fat and the risk of obesity-associated complications are provided in [A0024]. BMI as a single, relatively simplistic measurement of obesity does not reflect the whole complexity of the disease [169]. The European Association for the Study of Obesity (EASO) has called for an improvement in the classification of obesity by proposing revised ICD-11 diagnostic criteria based on three dimensions, namely aetiology, degree of adiposity, and health risks [169]. While the ICD-11 definition has been expanded to recognise the potential for increased adiposity to impair health, in line with the WHO definition, a classification system to support personalised disease management and practice changes has not yet been adopted [162, 166].

Target population

[A0007] – What is the target population of this assessment?

This is defined in the project Scope.

Briefly, the target population for this assessment is adults ≥18 years of age with a BMI ≥30 kg/m^2, specifically:

- BMI ≥40 kg/m^2, or
- BMI ≥35 kg/m^2 and comorbidities (for example, hypertension, diabetes), or
- BMI ≥30 kg/m^2 and type 2 diabetes (T2D) who have not achieved durable improvements in glycaemic control with reasonable non-surgical methods.

[A0023] – How many people belong to the target population?

The worldwide prevalence rates of overweight and obesity have increased steadily over time, approximately doubling since 1980 [170]. In 2010, the first OECD report on obesity estimated average rates of adult obesity in 31 OECD countries to be 21%. In 2016, the age-standardised prevalence of obesity among adults was estimated to be 24%, corresponding to approximately 50 million additional individuals [167]. Within Europe, obesity prevalence is variable between countries. In 2016, across 18 European countries (including Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, The Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, and the UK), the estimated age-standardised obesity prevalence for those 20–84 years ranged from 22.7% in Portugal to 29.3% in the UK for men, and from 19.5% in Switzerland to 31.3% in the UK for women [171]. Obesity rates are projected to continue to rise unless effective policy actions are put in place.

Not only is the prevalence of obesity increasing, but the degree of obesity among those with obesity is also increasing. Growth in severe and morbid obesity (BMI ≥35 kg/m^2 and BMI ≥40 kg/m^2, respectively) accounted for approximately 50% of the increase in obesity rates in OECD, G20, and EU28 countries between 2014 and 2016 [167]. In some countries, such as the United States, Saudi Arabia, and New Zealand, severe and morbid obesity accounted for over 70% of total obesity growth [167].

Among the consequences of the rising prevalence of obesity is the associated rise in cardio-metabolic comorbidities. Obesity has been associated with derangements of glycaemic, cardiovascular, and lipid parameters in numerous cross-sectional and cohort studies [172-175].

There are a number of challenges associated with estimating the prevalence of obesity. Much of the data is based on self-reported BMI measurements which are likely to produce biased estimates of weight status [176]. Furthermore, estimates of obesity prevalence based on WHO BMI cut-offs alone may not adequately capture the full scale of the problem when considering the role body fat distribution is known to play in prediction of cardio-metabolic disease risk [177].

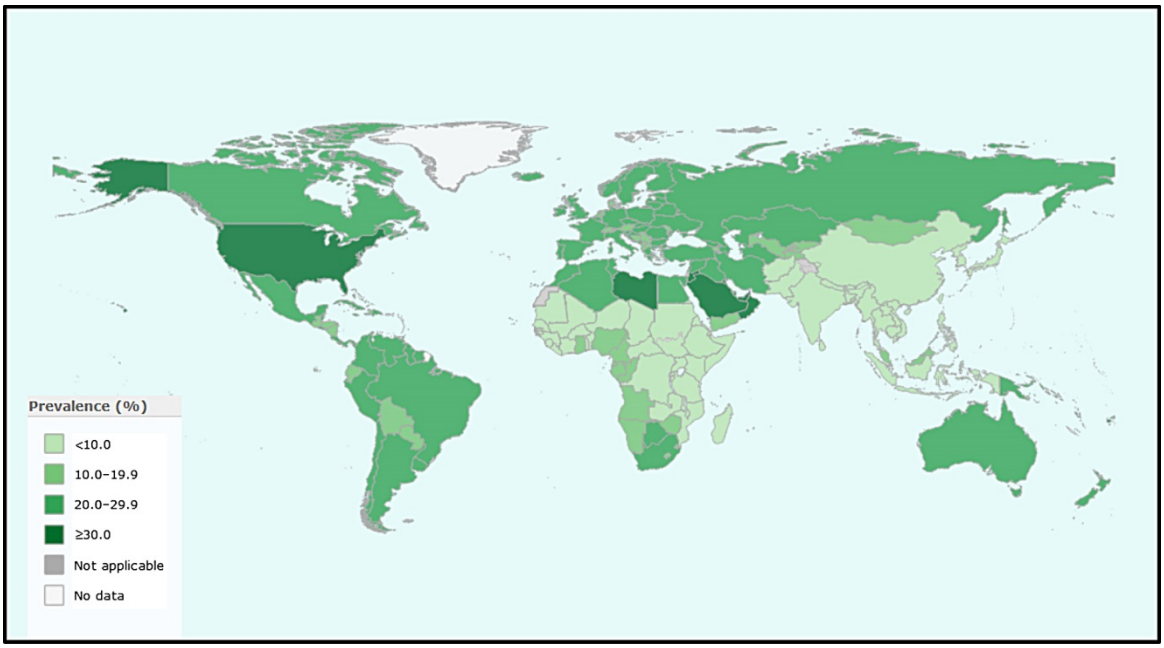


Figure 12: Global prevalence of obesity* among adults ≥18 years of age in 2016.

Source: Global Health Observatory [178]

* Body mass index ≥30 kg/m^2

[A0003] – What are the known risk factors for obesity?

There is substantial inter-individual variability in the association between certain risk factors and an individual's risk of developing obesity, however the fundamental cause is a sustained positive energy balance. Consumption of excessive calories beyond what is necessary to meet the body's energy requirements can lead to obesity, when sustained over a long period of time [170, 179].

Behavioural risk factors can include dietary patterns and physical activity. Additional contributing factors in our society or physical environment include education and skills, socioeconomic status and food marketing. These factors can be further categorised as modifiable (for example, diet or physical activity) or non-modifiable risk factors (for example, genetics or sex). Over time complex interactions between multiple behavioural, environmental and genetic factors can produce a positive energy balance [180, 181].

Some of the main modifiable and non-modifiable risk factors that increase the risk of obesity at a population level are outlined in Figure 13.

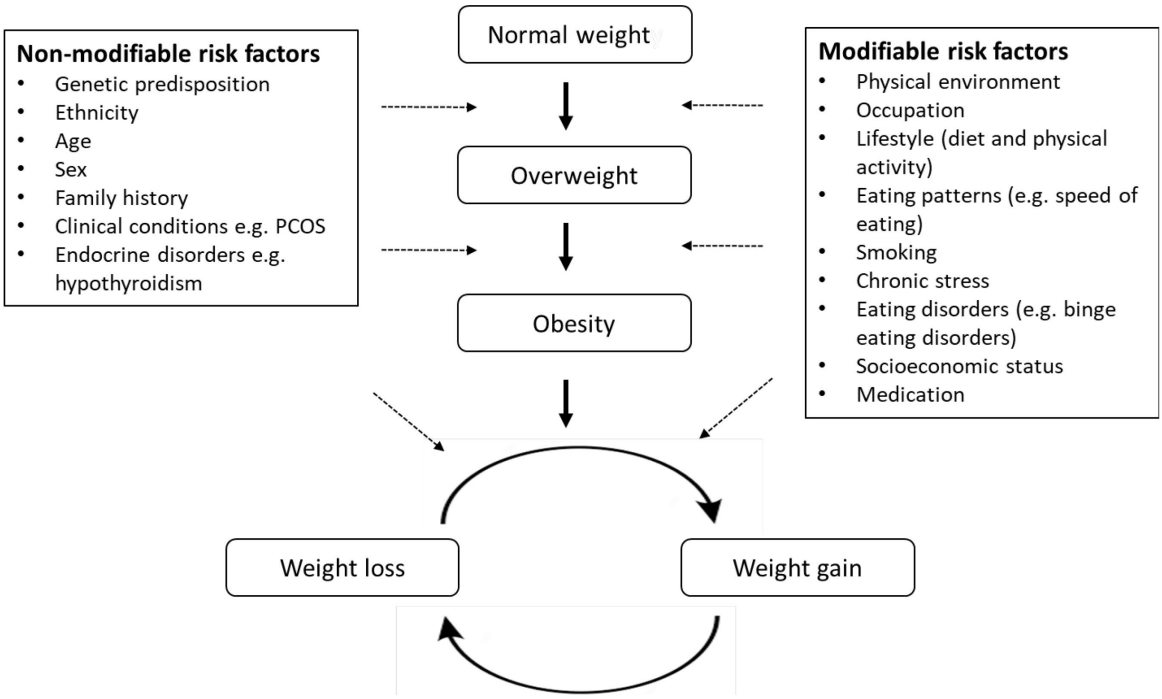


Figure 13: Modifiable and non-modifiable risk factors for the development of overweight and obesity.

Adapted from Durrer Schutz et al, 2019.[182]

Key: PCOS – Polycystic OvarY Syndrome.

Effects of the disease or health condition

[A0004] – What is the natural course of obesity?

Modifiable and non-modifiable aetiological factors described in [A0003] contribute to the progression from overweight (pre-obesity) to obesity over time. Obesity is associated with the development of a wide range of complications affecting many different aspects of physiology including T2D, cardiovascular disease (for example, stroke and coronary artery disease), respiratory disorders (for example, obstructive sleep apnea), musculoskeletal disorders (for example, osteoarthritis), obesity-related cancers and psychological impacts [167]. The risk of obesity-related complications increases with increasing BMI, particularly for those with obesity category II (BMI 35 to 39.9 kg/m^2) and morbid obesity (BMI ≥40 kg/m^2) [83].

A brief overview of common comorbidities and complications associated with obesity is outlined in Table 12 In addition, the metabolically healthy obese (MHO) phenotype is described.

Table 12: Obesity-associated comorbidities and complications.*

Body system or disease group	Complication or comorbidity
Cardiovascular system	Hypertension
	Dyslipidaemia (elevated triglycerides and decreased HDL cholesterol)
	Stroke
	Coronary heart disease (including ischaemic heart disease, angina pectoris and myocardial infarction)
	Pulmonary embolism
	Deep vein thrombosis
	Peripheral artery disease
Neurological disorders	Idiopathic intracranial hypertension (IIH)
Cancer	Breast cancer
	Oesophageal and gastro-intestinal cancers (i.e. oesophageal, small intestinal, colon, rectal, hepatic, gallbladder, pancreatic)
	Kidney cancer
	Cancers of the male reproductive system (e.g. prostate)
	Cancers of the female reproductive system (e.g. cervical, ovarian, endometrial)
Metabolic/endocrine	Type 2 diabetes and associated microvascular complications (nephropathy, neuropathy, retinopathy)
	Insulin resistance
	Metabolic syndrome†
	Hyperuricaemia and gout
	Non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), cirrhosis and associated complications (e.g. hepatocellular carcinoma)
	Endocrine disorders (e.g. polycystic ovary syndrome (PCOS))
Gastro-intestinal system	Gastro-oesophageal reflux disease (GERD)
	Herniation
	Gallstones
	Acute pancreatitis
Kidneys	Nephropathy or chronic kidney disease
Respiratory system	Obstructive sleep apnea
	Exertional dyspnoea
	Asthma
	Breathlessness
	Obesity hypoventilation syndrome (Pickwick syndrome)
Genitourinary system	Urinary incontinence
Musculoskeletal/orthopaedic disorders	Pain in the back, hips, ankles, feet and knees and associated reduced physical functioning
	Functional limitations (difficulty carrying out activities of daily living)
	Varicose veins
	Osteoarthritis
Psychological/psychosocial	Low self-esteem

Body system or disease group	Complication or comorbidity
complications	Body image disorder
	Anxiety
	Depression
	Social isolation and stigmatisation
Obstetric and perinatal complications	Pregnancy-related hypertension and preeclampsia
	Hyperglycaemia and gestational diabetes
	Adverse neonatal outcomes (e.g. fetal macrosomia)
Other	Reproductive disorders
	Reduced quality of life
	Higher risk of surgical complications
	Increased mortality risk

* Not an exhaustive list.

† The metabolic syndrome (MetS) is a group of five risk factors that increase the likelihood of developing cardiovascular disease and T2D including central obesity, hyperglycaemia, dyslipidaemia (raised triglycerides and lowered high-density lipoprotein cholesterol) and hypertension [183].

Source: KCE, 2019; WHO, 2007; Fruh, 2017 [75, 83, 184].

Metabolically Healthy Obesity

The WHO defines overweight and obesity as abnormal or excessive fat accumulation that presents a risk to health [162]. With consideration to the considerable inter-individual variability in the percent body fat for any given BMI value and the associated metabolic risk [170], a better approach may be to stratify patients according to clinical risk rather than obesity level as defined by BMI. While in general overweight and obesity are associated with an increased risk of obesity-related comorbidities, there is considerable inter-individual variability in the adverse health consequences of obesity. The metabolically healthy obese (MHO) phenotype refers to individuals with obesity with an adequate metabolic profile despite having excess body fat [185]. However, while the MHO phenotype includes those most resilient to the effects of obesity on cardio-metabolic outcomes, it is not a stable state and should not be considered a benign condition. Many individuals with MHO will eventually develop complications associated with obesity [185].

[A0005] – What are the symptoms and the burden of obesity for the patient?

The signs of overweight and obesity include a high BMI and central or abdominal distribution of body fat [186]. There are no specific symptoms of overweight and obesity [186]. However, individuals with overweight or obesity are more likely to develop chronic diseases that result in detrimental long-term consequences to their quality of life [167]. The symptoms of obesity vary from person-to-person and are highly dependent on the presence and severity of obesity-related complications such as T2D, obstructive sleep apnea, osteoarthritis, heart and vascular conditions as described in [A0004].

Day-to-day symptoms or problems can include breathlessness or dyspnoea on exertion, difficulty sleeping, tiredness and musculoskeletal pain resulting in reduced mobility [187]. Individuals may also experience psychological problems including low self-esteem, low confidence levels, feeling isolated or stigmatised in society which could lead to depression [187].

[A0006] – What are the consequences of obesity for society?

Obesity is associated with range of debilitating conditions such as T2D, cardiovascular diseases, osteoarthritis, respiratory difficulties and psychosocial problems, which lead to reduced life expectancy, reduced quality of life and disability [94]. However, the impact of obesity is not limited to population health and health service utilisation; the negative consequences of obesity are also costly in terms of lost productivity [167, 169].

In 2017, overweight and obesity were estimated to have caused 2.3 million deaths globally (95% uncertainty interval (UI) 1.4-3.4) in males and 2.4 million deaths in females (95% UI 1.6-3.4) [188]. Disability-adjusted life years (DALYs) attributable to overweight and obesity in males and females were 77.0 million (95% UI 49.7-108.2) 70.7 million (95% UI 49.1-94.9), respectively [188]. In 2017, cardiovascular disease was the leading cause of high-BMI-related death and DALYs, followed by diabetes and kidney disease [188].

The management and treatment of obesity-related comorbidities compared to normal-weight individuals entail increased health service utilisation across a range of health services [167], including increased primary care, inpatient and outpatient health services, as well as increased emergency department attendances and diagnostic testing [189-192]. Based on current epidemiological trends, between 2020 and 2050 OECD countries will spend 8.4% of their healthcare budget on treatment of complications associated with overweight and obesity [167]. It is estimated that excess adiposity will be responsible for, on average, 70% of all treatment costs for diabetes, 23% of treatment costs for cardiovascular diseases and 9% for cancers [167].

In addition to the direct costs of obesity associated with healthcare services utilisation, the additional indirect financial burden on society is significant. A systematic review examining the direct and indirect costs of overweight and obesity reported that over half of the total costs associated with obesity are attributable to indirect costs such as lost productivity and premature mortality [193].

Current clinical management of the disease or health condition

[A0024] – How is obesity currently diagnosed according to published guidelines and in practice?

Estimates of body fat including body mass index (BMI) and waist circumference measurement are used in everyday clinical practice in combination with a thorough medical assessment (including consideration of family history and lifestyle factors) to evaluate an individual's risk of obesity-associated complications.

Assessment of body fat

BMI is a simple and widely used measure used to classify overweight and obesity in adults in medical practice calculated by dividing an individual's weight in kilograms by the square of the height in metres (kg/m^2) [194]. BMI ranges have been assigned by the WHO as an estimate of adiposity in adults [194]. In general, as BMI increases so does the risk of complications related to excess adiposity (Table 13) [127, 194]. However, a BMI of ≥30kg/m^2 is not diagnostic of weight-related health problems. It is useful for generating population level estimates of overweight and obesity, however individuals with similar levels of obesity classified according to BMI may have different degrees of obesity-related complications [162].

Although it can generally be assumed that individuals with a BMI of ≥30 kg/m^2 have increased adiposity, BMI cannot distinguish between fat and muscle mass [195]. A given BMI does not correspond to the same degree of body fatness in all individuals and does not account for the wide variation in body fat distribution in different individuals and populations, therefore it may not accurately predict obesity-related health risk in some individuals [196]. The relationship between BMI and body fatness is variable dependent on age (BMI may not accurately predict body fatness in the elderly), sex (adiposity is higher in women than in men of equivalent BMI) and ethnicity (at the same BMI, Asian populations demonstrate more body fat than Caucasians) [195, 196]. Despite the limitations associated with the use of BMI criteria, in general, a BMI ≥30kg/m^2 is considered to be indicative of weight-related health risk in Caucasians. Table 13 shows a simplistic relationship between BMI and the risk of obesity-associated comorbidities for Caucasians, which can be affected by a range of factors, including diet and activity level [196]. It is recognised that ethnic groups differ in the level of risk associated with a particular BMI, precluding the development of globally applicable cut-off points. Different BMI thresholds are associated with an elevated risk of obesity-related complications for other ethnic groups [197].

Table 13: Weight-related risk of obesity-associated comorbidities based on WHO BMI ranges in CAUCASIANS [194].

WHO Classification	BMI (kg/m^2)	Risk of obesity-related complications
Underweight	<18.5	Low[†]
Normal range	18.5 – 24.9	Average
Overweight	25.0 – 29.9	Increased
Obese	≥30	
Obese class I	30.0 – 34.9	Moderate
Obese class II	35.0 – 39.9	High
Obese class III[‡]	≥40.0	Very high

Key: BMI – Body Mass Index; WHO – World Health Organisation.

* BMI thresholds are based on Caucasians. Specific BMI cut-offs are applied for other ethnic groups.

[†] The comorbidities associated with underweight are distinct from those associated with increased adiposity. At a BMI <18.5, the risk of other clinical problems is increased [196].

[‡] Commonly referred to as morbid or extreme obesity.

Source: World Health Organization 2000 [196]; Obesity Canada, the Canadian Association of Bariatric Physicians and Surgeons and the Canadian Institutes of Health Research 2020 [153].

Assessment of body fat distribution

Storage of excess fat in the intra-abdominal depots increases the risk of adverse cardio-metabolic health outcomes [196]. Thus, body fat distribution may be a more useful indicator of health risk than the absolute amount of body fat. Central or abdominal obesity, characterised by excess visceral adipose tissue, has several anthropometric proxies: waist circumference; waist-to-hip ratio and waist-to-height ratio (WHtR) which have been shown to be useful predictors of morbidity related to cardio-metabolic risk [164, 198]. Indicative cut-off points have been adopted by the WHO, NICE and the IDF [199-201]. A waist circumference of ≥94 cm and ≥80 cm in Caucasian men and women, respectively, carries an increased risk of adverse health outcomes [127, 196]. The WHO advises that a more accurate classification of obesity-related health risk for certain obesity-associated complications such as T2D and cardiovascular disease may be achieved using measures of central adiposity in addition to BMI (Table 14) [196].

Table 14: Sex-specific waist circumference and average risk of cardio-metabolic complications in CAUSCASIANS

Risk of cardio-metabolic complications	Waist circumference (cm)	
	Men	Women
Increased	≥94 cm	≥80 cm
Substantially increased	≥102 cm	≥88 cm

Source: WHO, 2008**;** WHO 2000; SIGN 2010; NICE 2014 [127, 161, 196, 200].

* BMI thresholds are based on Caucasians. Specific BMI cut-offs are applied for other ethnic groups.

It is recognised that populations differ in the level of risk associated with a particular waist circumference, precluding the development of globally applicable cut-off points [196]. A number of organisations, including the IDF and WHO, have taken ethnic differences into consideration in the development of waist circumference cut-points as indicators of metabolic risk [200, 201].

[A0025] – How is obesity currently managed according to published guidelines and in practice?

The management and treatment of obesity have wider objectives than weight loss alone and include clinical and psychosocial risk reduction.[202] As outlined in question [A0003], complex interactions between biological, behavioural, social and environmental factors are involved in the development of obesity. It follows that a multi-faceted approach including dietary, physical activity and behavioural/psychological interventions is necessary to manage obesity and produce weight loss (Table 15; Figure 14). At an individual level, management and specific treatments for obesity have to be aligned with the severity of the obesity, the medical risk factors, associated co-morbidities, and any functional limitations. Bariatric surgery is typically not considered as a first line intervention for patients with obesity. Even for bariatric surgery patients, adherence to lifestyle changes pre- and post-surgery is imperative to the success of the operation.

In 2019, a systematic overview of international evidence-based guidelines for the management of overweight and obesity (specifically in in primary care) identified 19 guidelines, although not all guidelines identified were relevant to this assessment (primary obesity prevention guidelines, obesity management in children, rescinded or subsequently updated guidance) [203]. According to the results of the systematic review, there was considerable agreement in international, evidence-based guidelines on the multidisciplinary management of overweight and obesity in primary care [203]. A number of updated guidelines published subsequent to the systematic review search were also identified [4, 7, 117, 126, 153, 204]. Guidance from Europe (EASO/IFSO [94]; OMTF-EASO [202]; EAES [4];) the US (ADA; USPTF [205]; AACE/ACE [206]; AACE/TOS/ASMBS [207]; AACE/ACE/TOS [207]; AHA/ACC/TOS [106]; ES [208]) Scotland (SIGN) [161], England (NICE) [127, 199], Canada [209] and Australia (NHMRC) was identified [210]. Most recently, updated bariatric surgery guidelines from the European Association for Endoscopic Surgery (EAES) were published in 2020, superseding the previous 2014 guidelines, to reflect the latest advances in obesity management [4].

The overall aim of obesity treatments is to achieve weight loss resulting in a reduction in health risks [202] through:

- promotion of weight loss (reduction in BMI and waist circumference; changes in body composition)
- weight maintenance and prevention of weight regain
- management of co-morbidities
- improving quality of life and well-being.

Organisation of care

Typically, initial lifestyle interventions are carried out at a primary care level [156]. According to guidelines from the Obesity Management Task Force (OMTF) of the European Association for the Study of Obesity (EASO), patients may be referred to specialist services if treatment goals are not achieved or sustained with intervention at a primary care level [202, 211].

Table 15: Multicomponent lifestyle therapy for the treatment of obesity.

Multicomponent lifestyle intervention			
Treatment	**Dietary intervention**	**Physical activity and exercise**	**Behavioural therapy**
	• Reduced-calorie healthy meal plan • Meal plans can include: Mediterranean, low-carb, low-fat, volumetric, high protein, vegetarian, VLCD, LCD. • Individualised daily calorie deficit based on personal and cultural preferences • Meal replacements • Very low-calorie diet is an option for selected patients and requires medical supervision.	• Aerobic physical activity progressing to >150 minutes/week performed on 3–5 separate days per week. • Resistance exercise: single-set repetitions involving major muscle groups, 2–3 times per week. • Reduce sedentary behaviour. • Individualise programme based on preferences and physical limitations.	• Self-monitoring (food intake, exercise, weight) • Goal setting • Education (face-to-face meetings, group sessions, remote technologies) • Cognitive restructuring • Problem-solving • Stimulus control • Stress reduction and management • Psychological evaluation, counselling, and treatment where appropriate
Support or clinical supervision	• Dietician • Input from MDT	• Exercise trainer/physical activity coach • Input from MDT • Occupational therapist, physiotherapist, orthopaedic surgeon, as appropriate)	• Clinical psychologist, psychiatrist • Health educator • Peer support groups

Key: LCD – low calorie diet; VLCD – very low calorie diet.

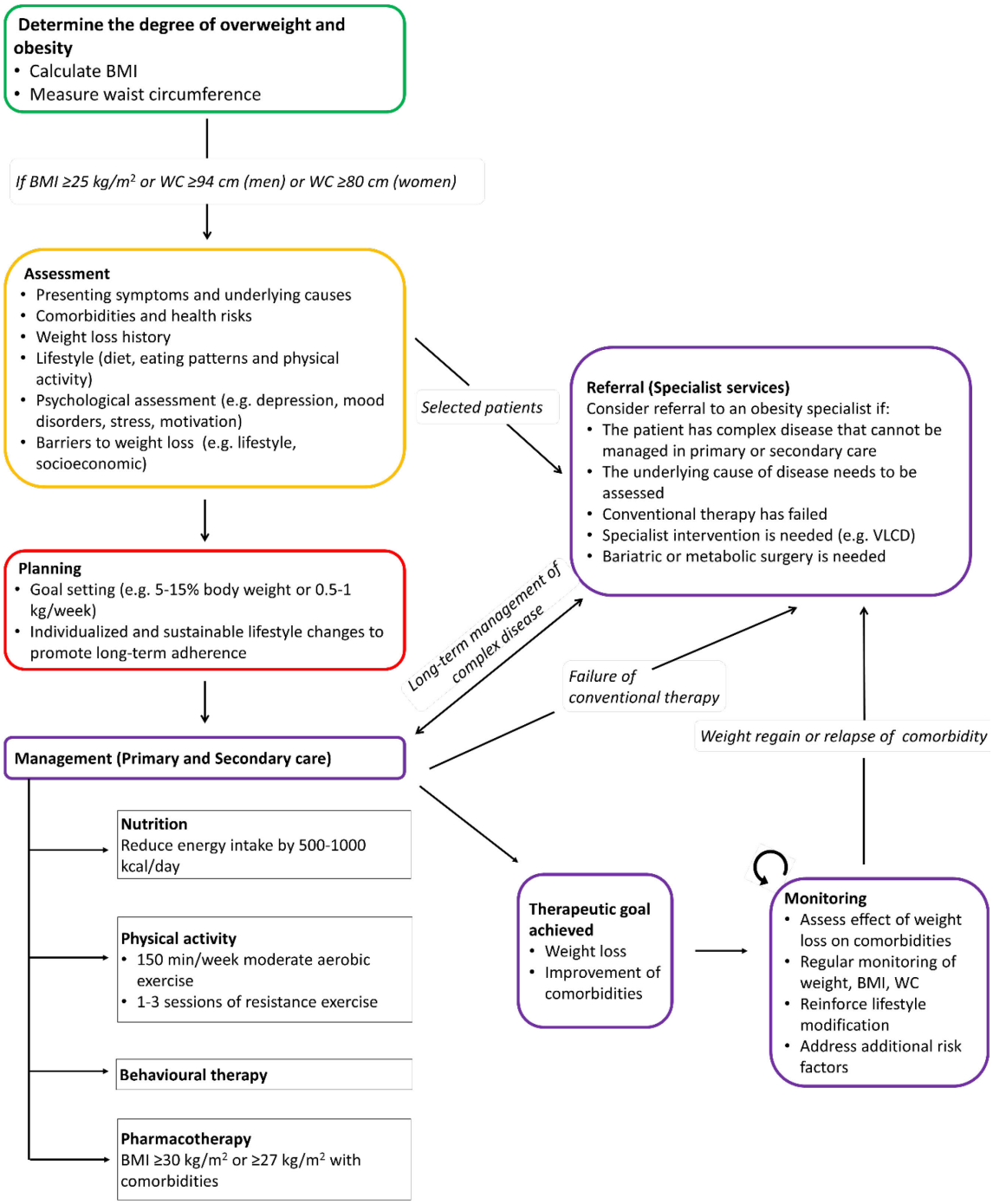


Figure 14: Proposed clinical care pathway for adults with overweight or obesity

Key: BMI – body mass index; WC – waist circumference; VLCD – very-low calorie diet.

* BMI and WC cut-off points are different for some ethnic groups.

Adapted from: EASO, 2015 [202].

EASO guidelines proposed a guide to assist in deciding the initial level of intervention for a particular patient depending on the severity of the obesity based on BMI and waist circumference measurement in addition to the presence of comorbidities (Table 16) [202]. Ultimately however, the selection of the most suitable intervention for an individual patient will depend on the results of clinical assessment and ability of the patient to adhere to the prescribed programme, with consideration given to previous weight loss attempts.

Table 16: Guide to selection of initial weight-loss intervention based on obesity severity and presence of comorbidities.

BMI (kg/m^2)*	Waist circumference (cm)*		Co-morbidities
	Men <94 Women <80	Men >94 Women >80	
25.0 – 29.9	L	L	L ± M
30.0 – 34.9	L	L ± M	L ± M ± S†
35.0 – 39.9	L ± M	L ± M	L ± M ± S
>40.0	L ± M ± S	L ± M ± S	L ± M ± S

Key: L – Lifestyle intervention; Medication – consider medication; S – consider surgery.

*BMI and waist circumference cut-off points are based on those recommended for Caucasian men and women according the IDF and WHO guidelines. Cut-off points are different for some ethnic groups.

†According to current guidelines for metabolic surgery, surgical intervention may be considered in some patients with BMI 30.0-34.9 kg/m^2 and obesity-related comorbidities on an individual basis, but is not currently recommended for all patients in this BMI category [4, 7, 85, 153].

Source: EASO, 2015 [202].

Lifestyle changes

Initial approaches to weight-loss and management of obesity-related comorbidities typically include dietary intervention, increased physical activity in addition to measures to support behavioural change and psychological support (Table 15; Figure 14) [94, 106, 153, 161, 202, 203, 212].

Pharmacological treatment

Anti-obesity drugs can be used to reinforce the patient's attempts to change eating behaviours and produce an energy deficit [202, 213], maintain weight-loss achieved through lifestyle modifications and may reduce or prevent the development of obesity-related co-morbidities depending on the mechanism of action [153, 214]. According to European and Candian guidelines, pharmacological intervention is recommended for patients with a BMI ≥30 kg/m^2 or a BMI ≥27 kg/m^2 with an obesity-related disease in addition to intensive lifestyle therapy [153, 202].

Bariatric or metabolic surgery

Bariatric or metabolic surgery is performed in combination with lifestyle and behavioural modifications in appropriately selected, fully informed patients [125]. Bariatric surgical procedures, described in detail in [B0001] and [B0002], are generally not recommended as a first-line approach in the treatment of obesity. Surgery is usually only considered for selected candidates after all other non-surgical interventions have failed to produce adequate weight loss and/or improvement in comorbidities, following a comprehensive interdisciplinary assessment [8, 202].

In recent years, revised bariatric/metabolic surgery recommendations have been published by a number of organisations including the ADA, EAES and Obesity Canada to expand indications to those with lower levels of obesity who do not achieve durable weight loss and improvement in comorbidities with nonsurgical methods (Figure 15) [4, 153]. According to these guidelines, laparoscopic bariatric surgery should be considered for patients with:

- BMI ≥ 40 kg/m^2, with or without comorbidities
- BMI ≥ 35 to 39.9 kg/m^2 with associated comorbidities
- BMI 30 to 34.9 kg/m^2 and T2D and/or arterial hypertension with poor control despite optimal medical therapy.

Long-term post-surgery follow-up and management of obesity, obesity-related diseases and any post-surgical complications is recommended to ensure optimal outcomes [85, 153]. The frequency of monitoring may be adjusted on an individual patient basis depending on attainment of treatment goals, compliance with necessary lifestyle adaptations and the expected nutritional complications associated with the bariatric/metabolic procedure [85, 126].

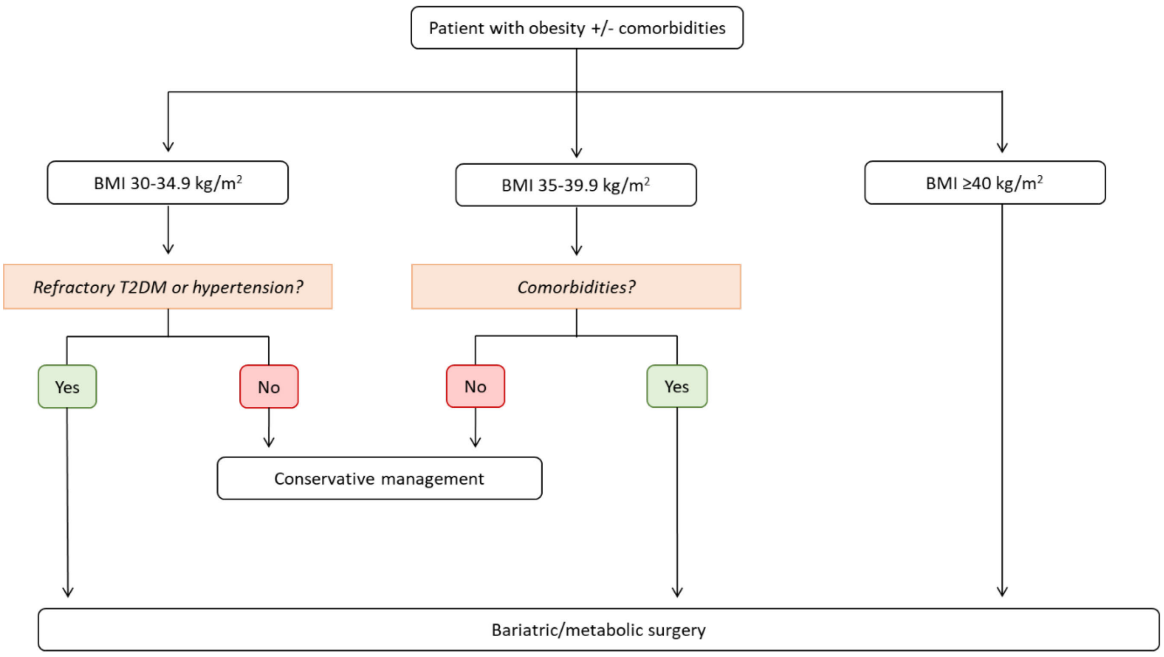


Figure 15: Proposed clinical pathway for selection of candidates for bariatric/metabolic surgery.

Adapted from Di Lorenzo 2020 [4].

[A0011] – How much are the technologies utilised?

No evidence was found to answer this research question.

5 CLINICAL EFFECTIVENESS (EFF)

5.1 Research questions

Element ID	Research question
D0001	What is the relative effect of the different bariatric surgical procedures on mortality?
D0005	What is the relative effect of the different bariatric surgical procedures on weight loss, and diabetes control?
D0006	What is the effect of the different bariatric surgical procedures on progression of obesity including the development or worsening of comorbidities?
D0011	What is the relative effect of the different bariatric surgical procedures on cardiovascular risk (e.g. diabetes, hypertension, hyper-lipidemia), GERD and micronutrient deficiency)?
D0012	Do the bariatric surgical procedures differ in their effect on generic health related quality of life?
D0013	Do the bariatric surgical procedures differ in their effect on disease specific quality of life?
D0017	Were patients satisfied with the technology?

5.2 Results

Included studies

For details on the study characteristics please see evidence tables included in Appendix 1.

We included 22 randomised controlled trials (RCTs) assessing the effectiveness of six different bariatric procedures for the treatment of obesity (SG, RYGB, D-RYGB, OAGB, BPD/DS, and AGB) and two combined procedures (B-SG, B-RYGB,). Results from these trials that had a follow-up period longer than 12 months were reported in 62 publications, published between 2006 and 2020. The study sample size ranged from 40 to 623 across studies (median: 87 participants). Twenty-one of these studies also reported SAF outcomes (see SAF section).

Country of origin

Fifteen studies were conducted in Europe: in Norway [32, 35, 47], France [48, 49, 63], Italy [28, 36, 53, 71], Sweden [42, 73], Finland [45], Belgium [46], the Netherlands [19], Germany [41], Switzerland [59], and Greece [50], respectively. Three studies originated in North America/USA [37, 56, 64], and two in South America: Brazil [62], and Mexico [30]. Two studies were conducted in Asia: India [67], and China [74].

Population

There were in total 3,179 participants in the 22 EFF studies. The mean age of participants ranged from 30.8 to 48.4 years (median: 41.8 years). The proportion of female participants ranged from 46.8% to 90.3% (median: 71.1%). Mean body weight ranged from 99.7 to 162.0 kg (median: 125 kg). Mean BMI ranged from 35,5 to 55,0 kg/m^2 across studies (median: 45,2 kg/m^2). Four studies included patients with a mean (or median) BMI corresponding to Class 2 obesity [37, 46, 64, 74], of which two included participants with T2D only [37, 64]. The remaining studies included patients with class 3 obesity, of which four studies included participants with a BMI>50 (super-obese) [32, 41, 42, 69].

Co-morbidities

Eighteen studies included people with T2D (range: 2.2%-100%; median:25%). Four of these studies included patients with T2D only [37, 53, 64, 73]. Four studies provided no information on whether participants with T2D were included. [37, 53, 64, 73]. The mean duration of T2D (7 studies reporting) among study participants ranged from 3.0 to 8.4 years [35, 37, 41, 53, 63, 64, 73],The proportion of participants with other comorbidities at baseline varied across studies as follows: hypertension (18 studies reporting) ranged from 7,6% to 73,5% (median: 46,4%); dyslipidemia (11 studies reporting) ranged from 0 to 88% (median: 55%); gastroesophageal reflux disease (GERD) (6 studies reporting) ranged from 6.6 to 46.4% (median: 16.3%); sleep apnea (10 studies reporting) ranged from 3.7% to 59% (median:21%), joint disease (3 studies reporting) ranged from 6% to 32%, and the proportion of people with metabolic syndrome (3 studies reporting) ranged from 65% to 94%.

Interventions and comparisons

The twenty-two EFF studies provided data for a total of 10 comparisons (see Table 17): 8 main comparisons and 2 which compared a standard procedure with a combined procedure (i.e. the same procedure but with an additional intervention constituting a gastric band or ring) [30, 41, 62, 71]. Eight of the studies compared SG with RYGB [19, 45, 48, 50, 59, 64, 73, 74]. Ten studies compared RYGB with other procedures: with BPD/DS [32, 42, 53]; AGB [28, 37, 56]; OAGB [63]; B-RYGB [30, 62], and D-RYGB [35]. One study compared SG with OAGB [67]; 1 study compared SG with AGB [46], and 2 studies compared B-SG with SG [41, 71]. None of the included studies assessed the effectiveness of SADI-S or SASI procedures.

Follow-up was at 2 years in 6 studies [19, 35, 62, 63, 69, 73], at 3 years in four studies [41, 46, 50, 67], at 4 years in 2 studies [42, 71], at 5 years in 8 studies [30, 32, 35, 37, 45, 48, 53, 59, 64]. Two studies provided data for 10 years follow-up [28, 56].

Table 17: Overview of comparisons

Comparisons (N = 11)	No of studies (N = 28)	No studies with SAF data only (FU ≤12 months)	No of participants (range)	Follow-up EFF studies, median years (range)
Comparisons with RYGB (6 comparisons; 23 studies)				
AGB vs. RYGB [28, 37, 56]	3	-	302 (46 to 197)	10 (5 to 10)
SG vs. RYGB [19, 36, 45, 47, 48, 50, 52, 58, 59, 64, 73, 74]	12	4	1,795 (49 to 623)	5 (2 to 5)
D-RYGB vs. RYGB [35]	1	-	123	2
OAGB vs. RYGB [40, 63]	2	1	313 (60 to 253)	2
BPD-DS vs. RYGB [32, 42]	2	-	107 (47 to 60)	4 (3 to 5)
BPD vs. RYGB [53]	1	-	40	5
B-RYGB vs. RYGB [30, 62]	2	-	460 (60 to 400)	3.5 (2 to 5)
Other comparisons with SG (4 comparisons; 5 studies)				
AGB vs. SG [46]	1		80	3
B-RYGB vs. SG [55]	1	1	114	-
B-SG vs. SG [41, 71]	2	-	144 (50 to 94)	3.5 (3 to 4)
OAGB vs. SG [67]	1	-	217	3

Outcomes

The types of outcomes reported in the included studies are summarised in Table A8. All studies reported one or more measure of weight change, and 16 studies reported one or more measure of T2D status. All but 3 studies reported on adverse events related to the surgery [19, 46, 52]. No study reported on the satisfaction of patients.

Settings

A total of 40 hospital sites or clinics participated in the included EFF studies. Fifteen studies included single sites. In studies with more than one site, the numbers were as follows: two [19, 32, 69], three [45, 73], sites [59], and nine sites [63].

Five of the 22 EFF studies reported annual hospital volumes per study site [19, 32, 35, 59, 63]. All 5 studies were conducted in high-volume settings (i.e. sites performing > 100 bariatric procedures/per year; [215]. The number of annual cases in these studies were as follows: > 500 RYGB and SG cases per year [19]; >200 RYGB procedures but only a total of 40 D-RYGB surgeries [69]; >150 annual cases [63], and several hundred RYGB procedures but only 15–18 BPD-DS procedures) [32]. In one study each centre had at least 10 years' experience in bariatric surgery and a minimum of 200 procedures performed per year [59]. None of the studies explicitly reported to have been conducted at private hospitals or clinics.

Surgeons

In 5 studies, the bariatric surgery was performed by a single surgeon [37, 50, 64], in one study by 2 surgeons [41], and/or by the same surgical team [68, 74]. In one study a total of 6 surgeons performed all interventions (each surgeon performed between 2 and 63 SG procedures, and between 3 and 60 RYGB procedures) [59]. Two studies described the procedures being performed by multiple surgeons [45, 63]. Five studies reported the personal experience of participating surgeons of different procedures [19, 28, 45, 59, 69] which was described as follows: at least 150 SG and 150 RYGB procedures performed [59];. ≥400 bariatric interventions performed (at each centre a maximum of 2 surgeons fulfilled this criteria) [59]; ≥200 procedures, mostly RYGB, performed [69], ≥150 LAGB surgeries performed, but only five LRYGB procedures [28]. One study described the surgeon as an experienced laparoscopists, without further detail on personal experience with the different procedures [45].

Study quality

Eighteen of the 22 EFF studies included were rated as being at high risk of bias, 3 at low risk [6], and 1 study [73] had an unclear risk of bias. For details see the risk of bias section.

Studies included in the NMA

The number of studies, surgical procedures and patients varied depending on the follow-up time and outcome. The numbers were as follows:

- 2 years follow-up, weight-related outcome:
  16 studies, 11 surgical procedures and 2.288 patients
- 3 years follow-up, weight-related outcome:
  14 studies, 7 surgical procedures and 1.361 patients
- 5 years follow-up, weight-related outcome:
  11 studies, 8 surgical procedures and 927 patients

- 2 years follow-up, T2D- related outcome:
  6 studies, 6 surgical procedures and 602 patients
- 3 years follow-up, T2D-related outcome:
  6 studies, 6 surgical procedures, and 666 patients
- 5 years follow-up, T2D-related outcome:
  5 studies, 5 surgical procedures, and 455 patients

Two studies [28, 56] comparing AGB and RYGB (N=256) provided data for 10 years follow-up but these were not included in the NMA.

Mortality

[D0001] – What is the relative effect of the different bariatric surgical procedures on mortality?

Based on the available data from included RCTs, the highest calculated relative risk of early death was found for BPD-DS, but this estimate had great uncertainty (wide CI). A smaller RR was found for RYGB, and SR-RYGB, with good precision of the estimated risk for RYGB. Due to limited available data we cannot determine the relative effect on early mortality across all surgical procedures under study. We also believe that register data would be a better source for answering this research question. As for the late deaths, the reporting was poor in many of the studies, with reasons and timing of death not reported, making it impossible to draw any conclusion regarding the relative effect of different procedures on late mortality.

Early and late deaths

The number of early and late deaths after the different bariatric procedures, and the reasons and timing of death, are summarised in Table 22 and Table 23. See also Figure 31. Nine of the 28 included studies [31, 42, 45, 57, 61-63, 68, 216] reported in total 20 deaths (for one it was not stated to which group it belonged). Three studies did not report whether any deaths had occurred during follow-up [19, 48, 49].

Early Deaths

Three studies [42, 61, 62] reported a total of 4 early deaths (< 30 d after the initial procedure). One in 53 people with a BMI>50 (super-obesity) died of a lung emboli 3 weeks after BPD-DS [42], two of 1,382 people who received RYGB died due to surgical complications (leaks, fistulas) that led to infections and multiple organ failure [61, 62], and 1 in 230 people died after receiving B-RYGB, also due to multiple organ failure [62]. Two of the 4 early deaths occurred in the same study [62]. This translates into 19 expected early deaths per 1,000 people after BPD-DS, 2 deaths per 1000 people after RYGB, and 4 deaths per 1,000 people after SR-RYGB. The RRs indicative only, when counts are not from the same randomised trial, which is a limitation with the computed RRs.

Table 18: Expected early deaths per 1,000 people (95%ci) after obesity surgery

Treatment	Extracted Data	Expected early deaths per 1,000 people (95% CI)
BPD-DS	1 early death/53 people	19 (1 to 101)
RYGB	2 early deaths/1,382 people	2 (1 to 6)
B-RYGB	1 early death/230 people	4 (1 to 24)

Table 19: Computed relative risks (95%ci) of early deaths

	BPD-DS	RYGB	B-RYGB
BPD-DS		13.0 (1.2 to 141.5)	4.3 (0.3 to 68.3)
RYGB			0.3 (0.0 to 3.7)
B-RYGB			
Relative risks (RR) and 95% CIs. RR > 1 favors the treatment specified by the column title.			

Late Deaths

Six studies [31, 61, 62, 68, 216] reported a total of 16 late deaths (>30 d after the initial procedure). Seven late deaths occurred after RYGB: two due to cancer [61, 216], two alcohol-related deaths [57], and three deaths of unknown reason [45, 62]. Three deaths after SG of which one was due to myocardial infarction [68], and the other due to unknown reason [45]. Three assumed late deaths were reported to have occurred in OAGB but with no information on the reasons or the timing of death provided (2 in [63] and 1 in [68]). Two deaths occurred after SR-RYGB, [62] but the reasons were somewhat unclear (2 deaths to cholelithiasis and one sudden death was reported, but unclear in which group).One study reported that one participant died of melanoma, but it was unclear if this person was part of the RYGB or the B-RYGB group [31]. This translates into 14 expected deaths/10,000 person-years in RYGB, 12 per 10,000 person-years in SG, 52 per 10,000 person years in OAGB, and 36 per 10,000 person years in B-RYGB,

Morbidity

[D0005] – What is the relative effect of the different bariatric surgical procedures on weight-related outcomes, and diabetes control?

The results of the NMAs, for both weight-related outcomes and diabetes control suggest little or no differences between procedures, but these results are of low to very low quality. There is a lack of studied with long term follow-up; in particular for patients with BMI 30-35 and uncontrolled T2D, the evidence is scarce overall.

Weight-related outcomes

Two years follow-up

Seventeen studies provided data on this outcome at 2 years follow-up suitable to be transformed to SMD according to our ranking method [19, 28, 35, 37, 41, 42, 45, 48, 53, 56, 59, 62, 64, 68, 71, 73, 74]. The network includes 9 surgical procedures. Mean study BMI ranged from 35.5 (RYGB vs AGB) [37] to 55 (RYGB vs BPD-DS) [32]. The network architecture is displayed in Figure 16.

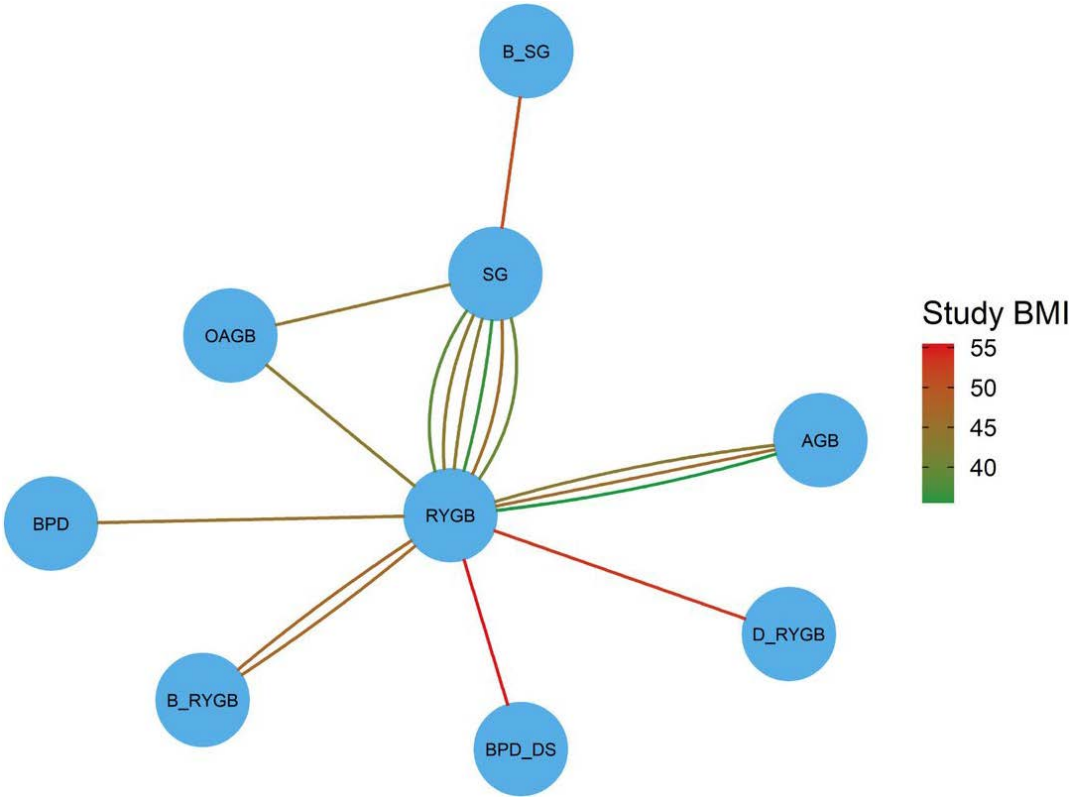


Figure 16: Network 2 years follow-up SMD-weight-related outcome

Surgical procedures included in the NMA. Each line represents a single study. Studies are coloured according to their study BMI. Comparisons between two surgical procedures connected with a line are called direct comparisons. In case no direct connection is available we speak of indirect comparisons.

Abbreviations: AGB: adjustable gastric banding; B-RYGB: banded Roux-en-Y gastric bypass; B-SG: banded sleeve gastrectomy; BPD: biliopancreatic diversion; BPD-DS: biliopancreatic diversion with duodenal switch; D-RYGB: distal Roux-en-Y gastric bypass; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

The results showed largely similar effects of the individual surgical procedures. The SUCRA plot indicates a higher probability for BPD-DS to rank first (61%) compared to the other surgical procedures (all below 10%). The high-ranking probability for BPD-DS might be explained by the high study BMI which might contribute to a better ranking due to heterogeneity. However, according to the 95% credibility intervals (CrI) none of the surgical procedures showed superiority compared to RYGB. The results were robust in terms of whether the random effect or the fixed effect model was used. The nodesplit analysis showed no signs of inconsistency (all p values > 0.81), See Appendix 5: Supplementary NMA results, Figure A5 and Figure A6. For further details on the fixed effect model see Appendix 5, Outcome weight, Two years follow-up.

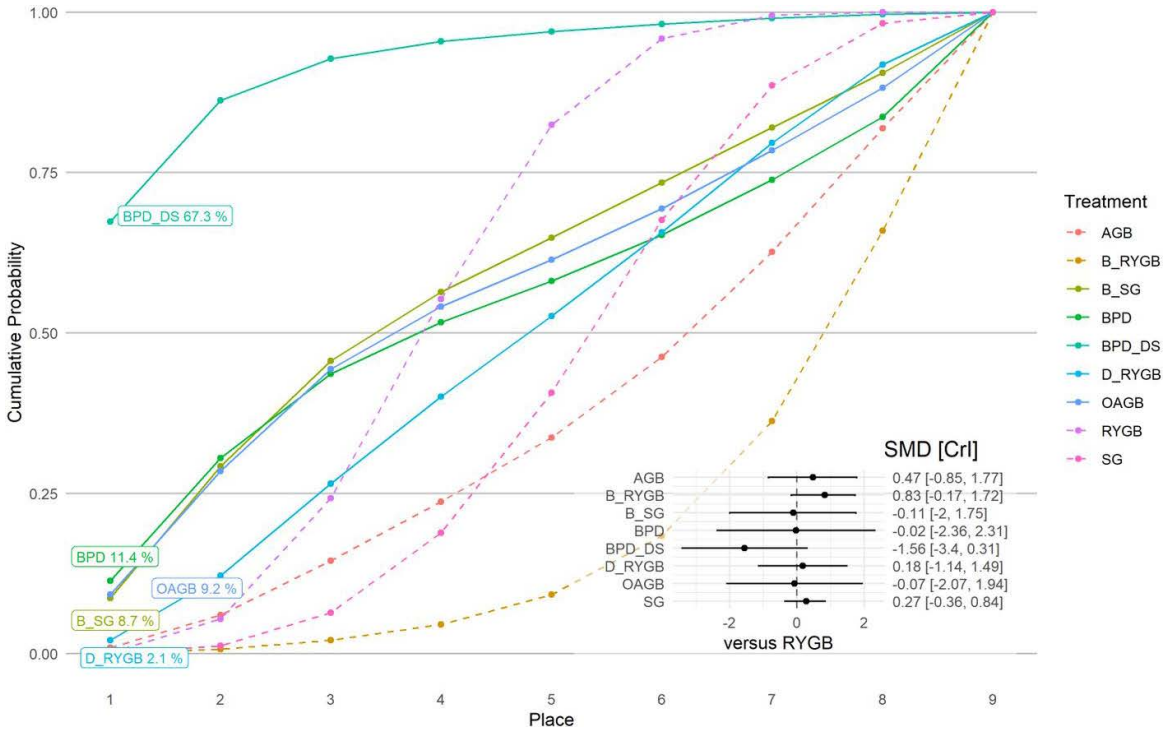


Figure 17: SUCRA and Forest Plot SMD-weight-related outcome at 2 years follow-up (random effects model)

SUCRA (coloured plot): Surgical procedures are displayed according to their probability to achieve a specific rank (or better). In specific, BPD-DS has a 61% probability to rank first and BPD a 9.9% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual surgical procedures might achieve a high-ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is only judged to be relevant if the credibility intervals of the forest plots show superiority.

Abbreviations: AGB: adjustable gastric banding; B-RYGB: banded Roux-en-Y gastric bypass; B-SG: banded sleeve gastrectomy; BPD: biliopancreatic diversion; BPD-DS: biliopancreatic diversion with duodenal switch; D-RYGB: distal Roux-en-Y gastric bypass; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

Three years follow-up

Fourteen studies provided weight-related data at 3 years follow-up suitable to be transformed to SMD according to our ranking method [28, 37, 41, 42, 45, 46, 48, 50, 56, 59, 64, 68, 71, 74]. The network includes 6 surgical procedures. Mean study BMI ranged from 35.5 (RYGB vs AGB) [37] to 54.5 (RYGB vs BPD-DS) [42]. The network architecture is displayed in Figure 18.

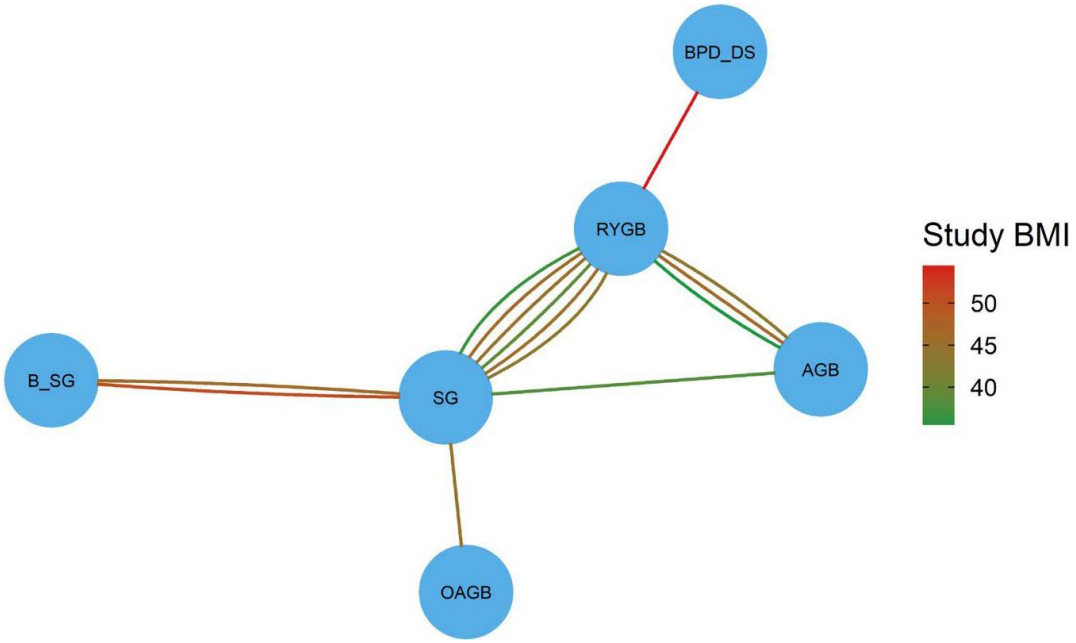


Figure 18: Network 3 years follow-up SMD-weight-related outcome

Surgical procedures included in the NMA. Each line represents a single study. Studies are coloured according to their study BMI. Comparisons between two surgical procedures connected with a line are called direct comparisons. When no direct connection is available, we speak of indirect comparisons.

Abbreviations: AGB: adjustable gastric banding; B-SG: banded sleeve gastrectomy; BPD-DS: biliopancreatic diversion with duodenal switch; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

The results were mostly similar between the individual surgical procedures in the random effects model Figure 19). According to the 95% credibility intervals (CrI) none of the surgical procedures showed a clear benefit compared to RYGB. Additionally, the ranking probabilities were largely similar. The fixed effect model indicated a benefit of AGB (SMD: -1.58, CrI: -2.77; -0.39) compared to RYGB. The consistency analysis shows strong signs of inconsistency in the AGB – RYGB – SG loop (all p values < 0.007). See Appendix 5, Figure A10 and Figure A11. For further details on the fixed effect model, see Appendix 5, Outcome weight, Three years follow-up.

BPD-DS now shows a worse mean effect size compared to RYGB (at 2 years follow-up BPD-DS had the best mean effect size). The change is caused by different studies included at the individual follow-ups. Overall, we were not able to detect meaningful differences between the individual surgical procedures at 3 years follow-up.

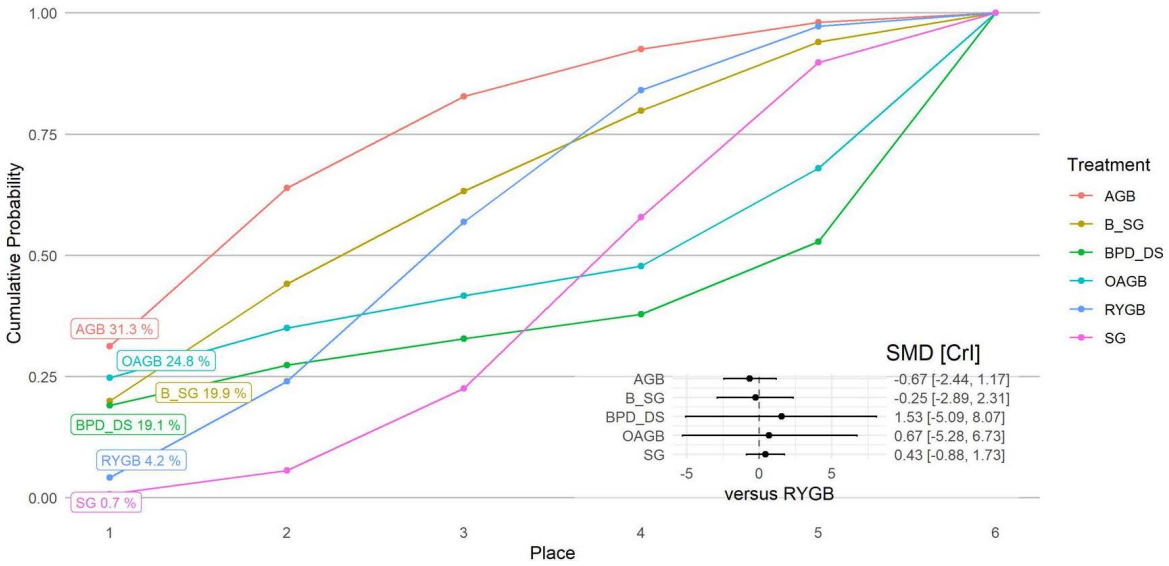


Figure 19: SUCRA and Forest Plot SMD-weight-related outcome at 3 years follow-up (random effects model)

SUCRA (coloured plot): Surgical procedures are displayed according to their probability to achieve a specific rank (or better). In specific, AGB has 43.9% probability to rank first and OAGB a 20.5% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual surgical procedures might achieve a high-ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is judged to be relevant only if the credibility intervals of the forest plots show superiority.

Abbreviations: AGB: adjustable gastric banding; B-SG: banded sleeve gastrectomy; BPD-DS: biliopancreatic diversion with duodenal switch; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

Five years follow-up

Eleven studies provided weight-related data at 5 years follow-up suitable to be transformed to SMD according to our ranking method [28, 30, 32, 35, 37, 45, 48, 53, 59, 64, 74]. The network includes 7 surgical procedures. Mean study BMI ranged from 35.5 (RYGB vs AGB) [37] to 55 (RYGB vs BPD-DS) [32]. The network architecture is displayed in Figure 20.

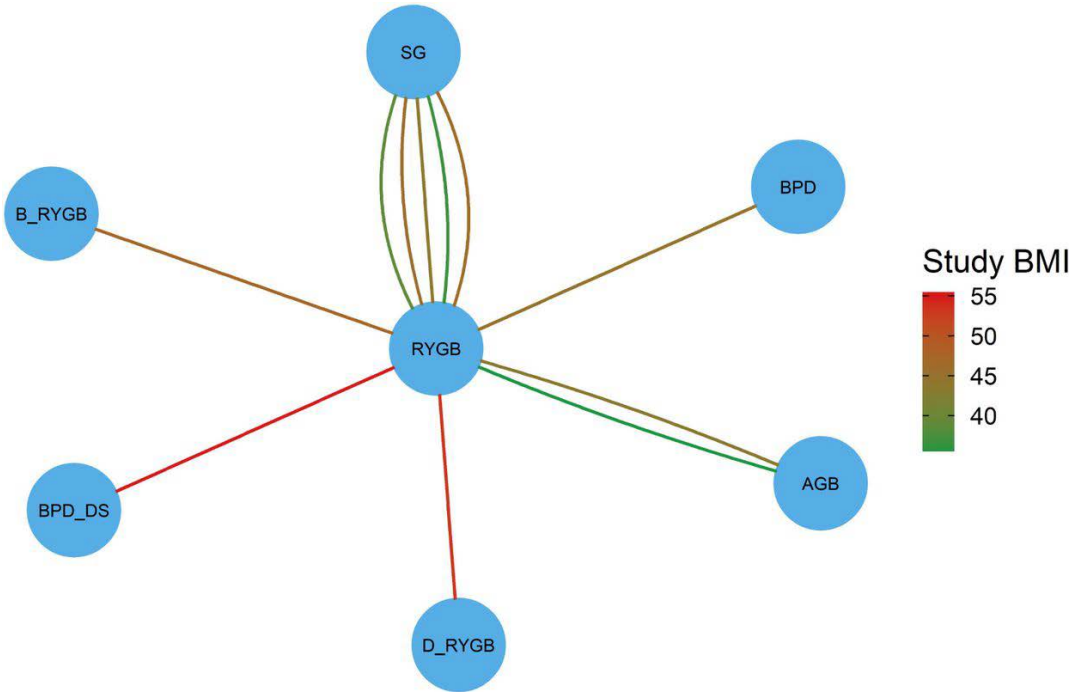


Figure 20: Network 5 years follow-up SMD-weight-related outcome

Included surgical procedures in the NMA. Each line represents a single study. Studies are coloured according to their study BMI. Comparisons between two surgical procedures connected with a line are called direct comparisons. When no direct connection is available, we speak of indirect comparisons.

Abbreviations: AGB: adjustable gastric banding; B-RYGB: band to Roux-en-Y gastric bypass; BPD: biliopancreatic diversion; BPD-DS: biliopancreatic diversion with duodenal switch; D-RYGB: distal Roux-en-Y gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

Aside from BPD-DS the results of the surgical procedures were largely similar (See Appendix 5, Figure A15). BPD-DS showed a higher probability of better ranks compared to other types of obesity surgery. The reason why this probability for BPD-DS changed again is that the results for five years follow-up derive from the same trial as from 2 years follow-up [32], whereas the 3 years follow-up results were from another study [42]. However, according to the 95% CrI, none of the surgical procedures showed a clear benefit compared to RYGB. The results remained similar regardless whether the fixed effect or random effects model was used. For further information, see Appendix 5, outcome weight, 5 years follow-up.

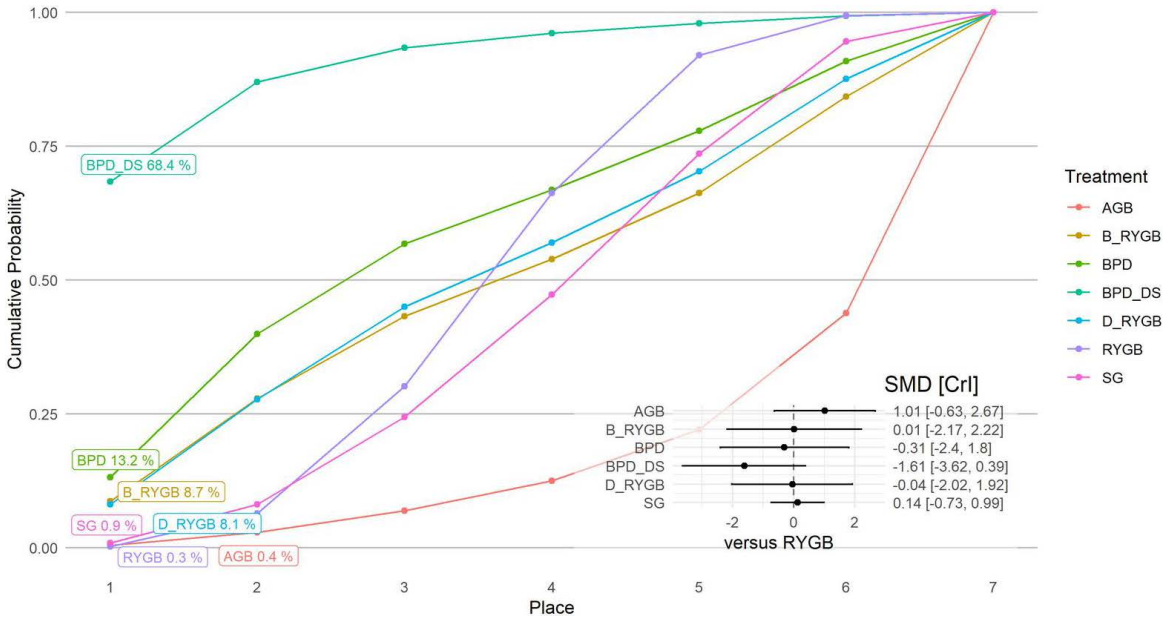


Figure 21: SUCRA and Forest Plot SMD-weight-related outcome at 5 years follow-up (random effects model)

SUCRA (coloured plot): Surgical procedures are displayed according to their probability to achieve a specific rank (or better). In specific, BPD-DS has 66% probability to rank first and BPD a 12.8% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual surgical procedures might achieve a high-ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is only judged to be relevant if the credibility intervals of the forest plots show superiority.

Abbreviations: AGB: adjustable gastric banding; B-RYGB: band to Roux-en-Y gastric bypass; BPD: biliopancreatic diversion; BPD-DS: biliopancreatic diversion with duodenal switch; D-RYGB: distal Roux-en-Y gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

Ten years follow-up

Two studies [28, 56] comparing AGB with RYGB provided weight data at 10 years follow-up (data not included in the NMAs). Results of both studies suggest superiority of RYGB in terms of weight loss. The studies reported greater mean%EWL (69±29% vs. 46±27%, p<0.03) [28], and greater mean total body weight loss (-42.4±19.6kg vs.-27.4±14.5kg) [56] in patients with RYGB as compared to patients with AGB.

Diabetes (TYPE 2)

Two years follow-up

Seven studies provided diabetes data at 2 years follow-up suitable to be transformed to SMD according to our ranking method [35, 37, 53, 63, 64, 67, 73].The network includes 6 surgical procedures. Mean study BMI ranged from 35.5 (RYGB vs AGB) [37] to 53.45 (RYGB vs D-RYGB) [35]. The network architecture is displayed in Figure 22.

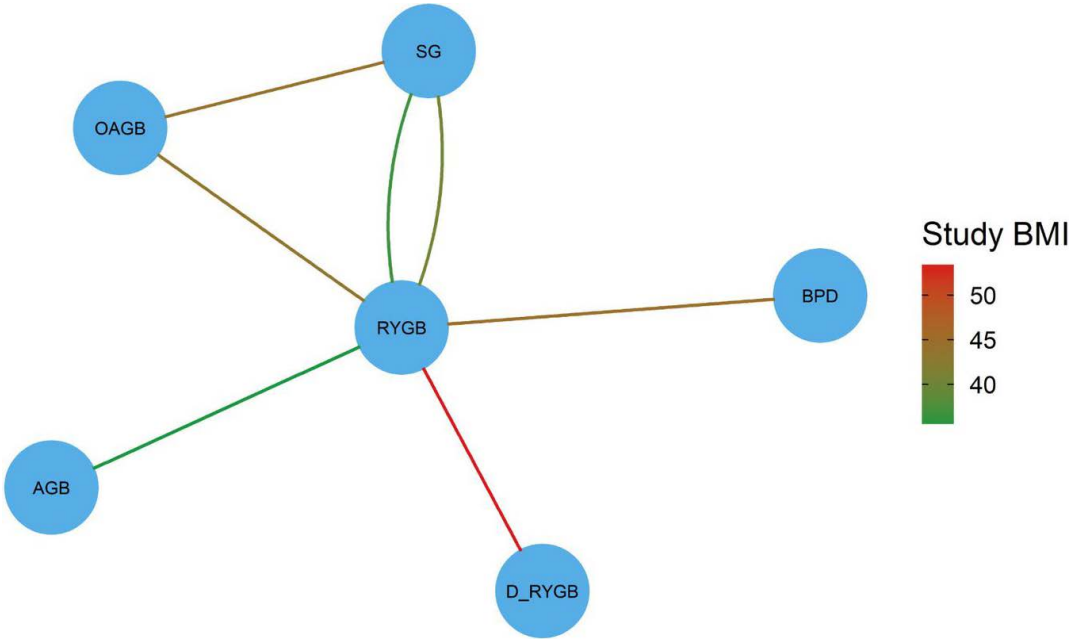


Figure 22: Network 2 years follow-up SMD-diabetes

Surgical procedures included in the NMA. Each line represents a single study. Studies are coloured according to their study BMI. Comparisons between two surgical procedures connected with a line are called direct comparisons. When no direct connection is available, we speak of indirect comparisons.

Abbreviations: BPD: biliopancreatic diversion; D-RYGB: distal Roux-en-Y gastric bypass; AGB: adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

Aside from BPD (SMD: -1.32, CrI: -2.13; -0.53), all surgical procedures showed equivalent performances in the random effects models (Figure 23). In the fixed effect model, D-RYGB as well as OAGB were also superior to RYGB (SMD: -0.26, CrI: -0.46; -0.06 and SMD: -0.58, CrI: -0.73; -0.43, respectively). The superiority these surgical procedures were not related to superior weight outcomes. Hence, these might be spurious finding. The nodesplit analysis showed no signs of inconsistency (all p values > 0.95). See Appendix 5, Figure A17 and Figure A19. For further information, see Appendix 5, outcome diabetes, 2 years follow-up.

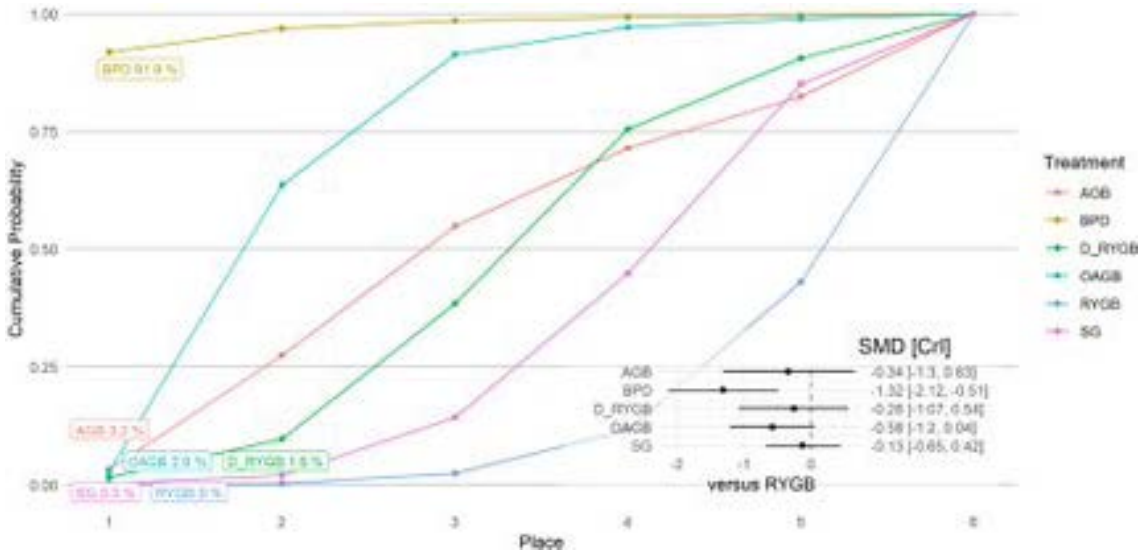


Figure 23: Sucra and forest plot SMD-diabetes at 2 years follow-up (random effects model)

SUCRA (coloured plot): Surgical procedures are displayed according to their probability to achieve a specific rank (or better). In specific, BPD has 92.1% probability to rank first and AGB a 3.1% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual surgical procedures might achieve a high ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is judged to be relevant only if the credibility intervals of the forest plots show superiority.

Abbreviations: BPD: biliopancreatic diversion; D-RYGB: distal Roux-en-Y gastric bypass; AGB: adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

Three years follow-up

Six studies provided diabetes data at 3 years follow suitable to be transformed to SMD according to our ranking method [37, 41, 42, 45, 66, 68]. The network includes 6 surgical procedures. Mean study BMI ranged from 35.5 (RYGB vs AGB) [37]) to 54.5 (RYGB vs BPD-DS) [42]. The network architecture is displayed in Figure 24.

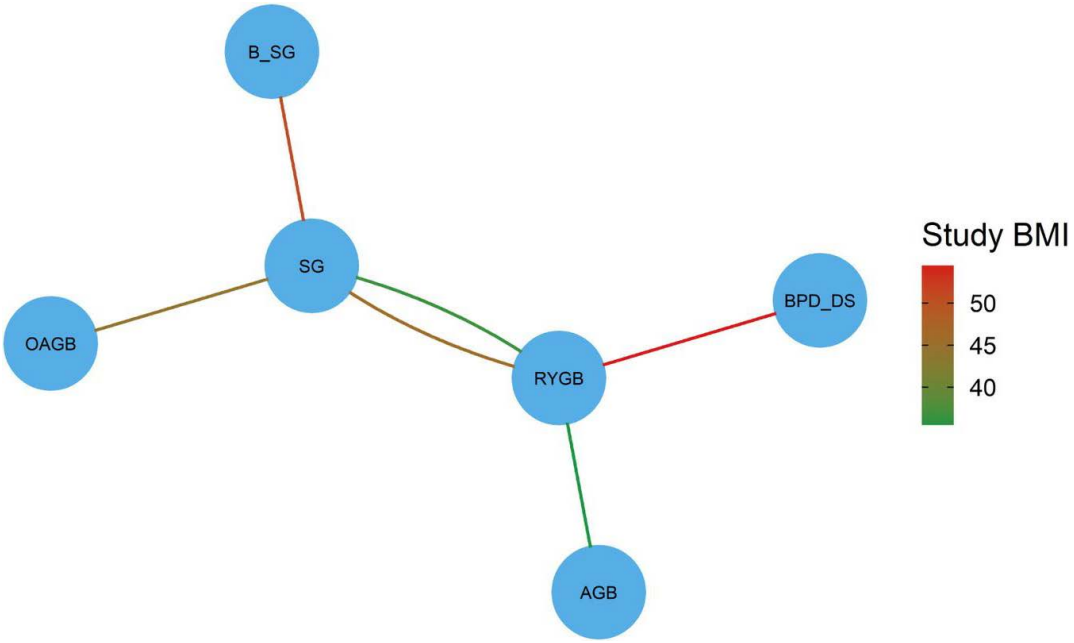


Figure 24: Network 3 years follow-up SMD-diabetes

Surgical procedures included in the NMA. Each line represents a single study. Studies are coloured according to their study BMI. Comparisons between two surgical procedures connected with a line are called direct comparisons. When no direct connection is available we speak of indirect comparisons.

Abbreviations: B-SG: banded sleeve gastrectomy; BPD-DS: biliopancreatic diversion with duodenal switch; AGB: adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

All surgical procedures showed largely equivalent performances in the random effect's models (Figure 25). The fixed effect model showed improved efficacy of OAGB compared to RYGB (SMD: -0.55; CrI: -0.82; -0,27). However, it seems unlikely that individual surgical procedures might have an effect on diabetes but not on weight. Due to the lack of closed loops a consistency analysis was not possible. See Appendix 5, Figure A22. For further information, see Appendix 5, outcome diabetes, 3 years follow-up.

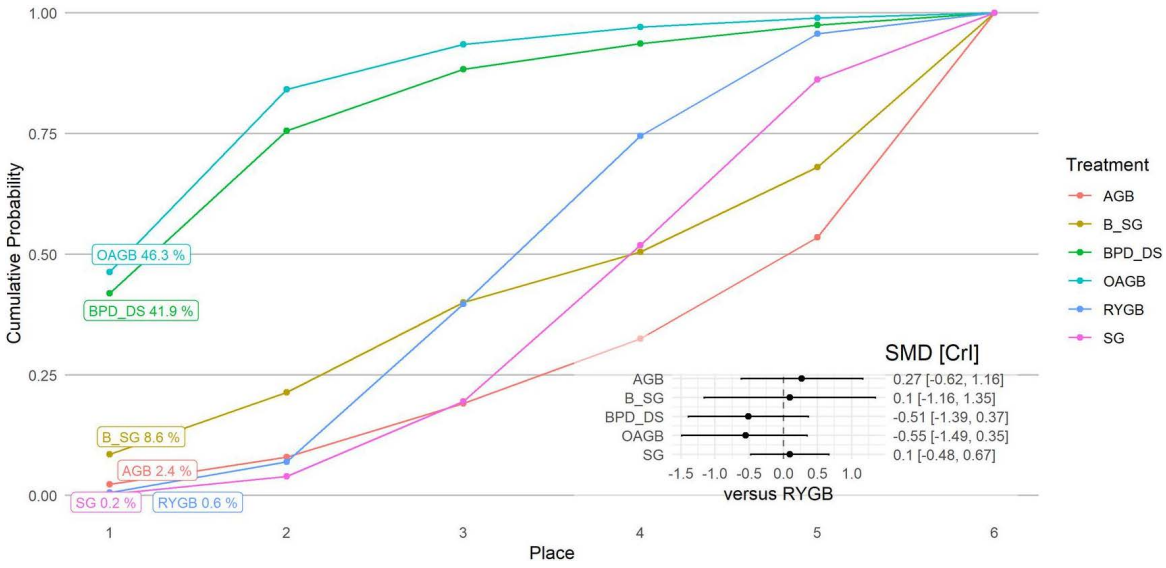


Figure 25: Sucra and forest plot SMD-diabetes at 3 years follow-up (random effects model)

SUCRA (coloured plot): Surgical procedures are displayed according to their probability to achieve a specific rank (or better). In specific, OAGB has 46.9% probability to rank first and BPD-DS a 41.5% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual surgical procedures might achieve a high-ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is judged to be relevant only if the credibility intervals of the forest plots show superiority.

Abbreviations: B-SG: banded sleeve gastrectomy; BPD-DS: biliopancreatic diversion with duodenal switch; AGB: adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

Five years follow-up

Five studies provided diabetes data at 5 years follow suitable to be transformed to SMD according to our ranking method [35, 37, 45, 53, 64].The network includes 5 surgical procedures. Mean study BMI ranged from 35.5 (RYGB vs AGB) [37] to 53.45 (RYGB vs D-RYGB) [35]. The network architecture is displayed in Figure 26.

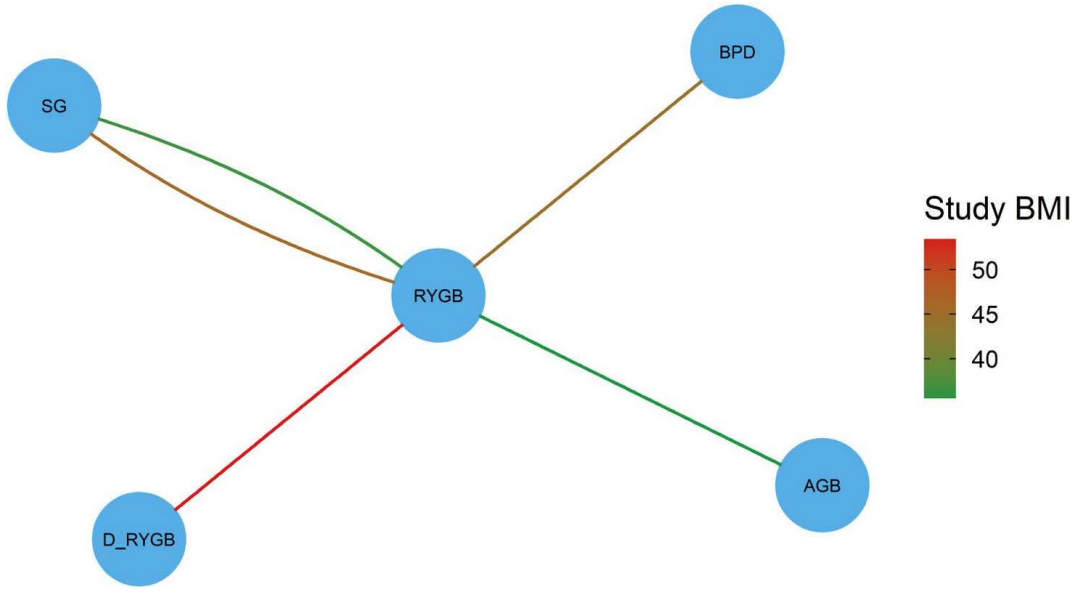


Figure 26: Network 5 years follow-up SMD-diabetes

Surgical procedures included in the NMA. Each line represents a single study. Studies are coloured according to their study BMI. Comparisons between two surgical procedures connected with a line are called direct comparisons. When no direct connection is available we speak of indirect comparisons.

Abbreviations: BPD: biliopancreatic diversion; D-RYGB: distal Roux-en-Y gastric bypass; AGB: adjustable gastric banding; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

The random effects model showed no clear superiority of any surgical procedure compared to RYGB (Figure 27). The fixed effect model indicated a superiority of BPD and D-RYGB compared to RYGB (SMD: -0.66, CrI: -0.84; -0.48 and SMD: -0.31, CrI: -0.51; -0.11, respectively). However, due to the risk of heterogeneity, the fixed effect model needs to be considered with caution. Additionally, it is still unclear why specific surgical procedures should have an effect on diabetes outcomes but not on weight. Due to the lack of closed loops, we were not able to conduct a nodesplit analysis. See Appendix 5, Figure A25. For further information, see Appendix 5, outcome diabetes, 5 years follow-up.

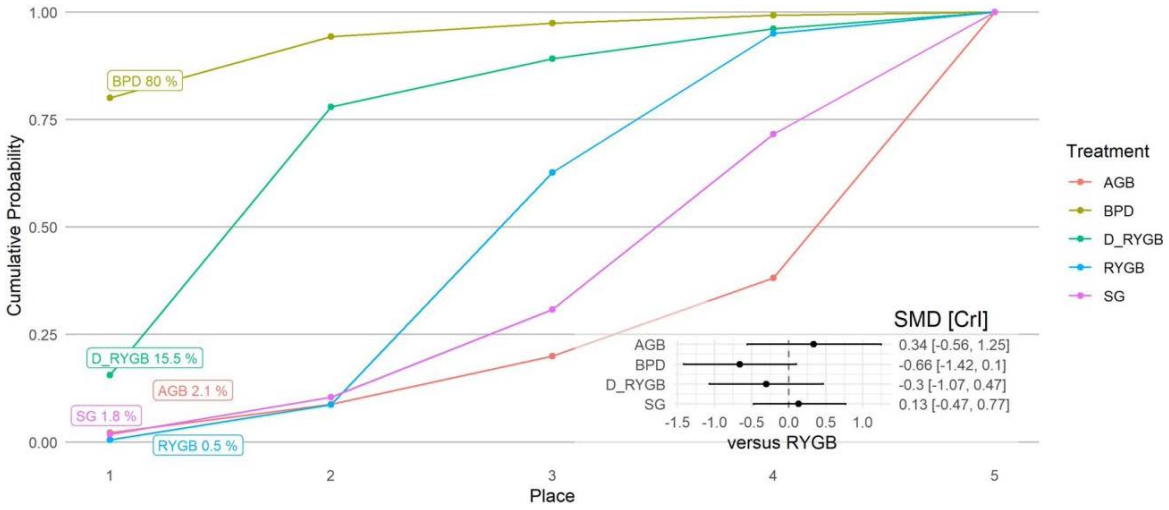


Figure 27: Sucra and forest plot SMD-diabetes at 5 years follow-up (random effects model)

SUCRA (coloured plot): Surgical procedures are displayed according to their probability to achieve a specific rank (or better). In specific, BPD has 80% probability to rank first and D-RYGB a 15.6% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual surgical procedures might achieve a high ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is judged to be relevant only if the credibility intervals of the forest plots show superiority.

Abbreviations: BPD: biliopancreatic diversion; D-RYGB: distal Roux-en-Y gastric bypass; AGB: adjustable gastric banding; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

[D0006] – What is the effect of the different bariatric surgical procedures on progression of obesity including the development or worsening of comorbidities?

The available evidence is insufficient to determine the relative effect on progression of obesity and worsening of comorbidities across all surgical procedures, as, for many comparisons and outcomes, only single studies provide data. Pooled data (3 studies), however, suggest (i) a greater risk of severe GERD (both existing and de novo), requiring conversion surgery, after SG than after RYGB, and (ii) a greater risk of insufficient weight loss and conversion surgery after AGB than after RYGB.

Eight of the 28 included studies (5 comparisons) provided data on weight regain from nadir, with nadir being defined as the lowest weight achieved after surgery [28, 32, 41, 53, 59, 62, 64, 74]. Seven studies (3 comparisons) provided data on inadequate weight loss after obesity surgery requiring conversion [28, 37, 46, 48, 56, 59, 67].

AGB vs. RYGB

One study [29] reported a weight regain around 2 years after surgery (nadir weight) in both the AGB and RYGB group, in kg (6.5±6.8 kg vs. 6.8 ± 7.4 kg), BMI units (3±3 kg/m^2 vs. 2±1 kg/m^2), and%EWL (10% ± 9% vs. 10% ± 11%) in respective group, up to 10 years follow-up. There were no differences in weight regain between groups. The weight at 5 years was significantly lower in RYGB than in the AGB (RYGB: 84 kg; AGB:97.9 kg).

Risk of conversion surgery due to insufficient weight loss

Pooled results of 2 studies [28, 56] showed greater risk of conversion surgery due to insufficient weight loss for AGB as compared to RYGB (RR: 11.10 [1.45, 85.08]). See Figure 28.

In 1 study [28], 4 patients in the AGB group received conversion surgery of which 2 to BPD and 2 to RYGB. In 1 study [56], 4 AGB patients received conversion to SG and 1 patient to RYGB. In a third study [37], the reason for conversion was not clear (and the conversion procedure unknown). Insufficient weight loss (treatment failure) was in 1 study defined as EWL <20% and the need for conversion surgery to another bariatric procedure [56], and in another study [28], insufficient weight loss was described as BMI >35 kg/m² at 5 yrs.

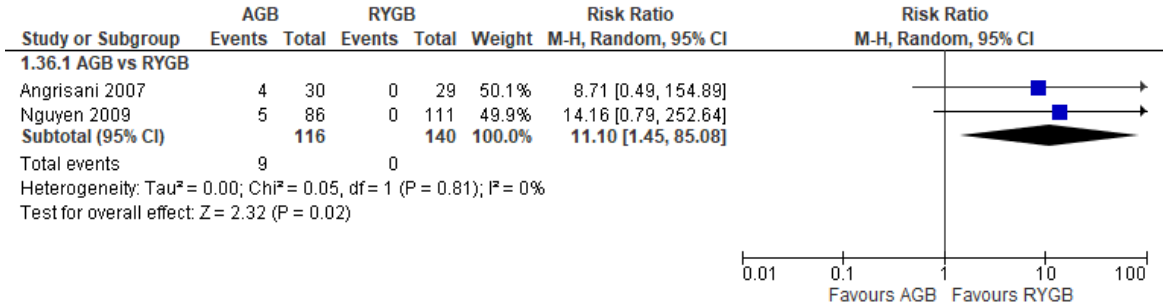


Figure 28: Risk of conversion surgery due to insufficient weight loss: Comparison: AGB vs. RYGB

Footnotes: AGB: adjustable gastric banding; RYGB: Roux-en-Y; CI: confidence interval. An RR>1 indicate a greater risk.

SG vs. RYGB

Two studies [59, 74] reported that nadir weight was reached between 1 and 2 years after both RYGB and SG, but no further information on weight gain was reported. One study reported no occurrence of excess weight gain, defined as a 5% increase in body weight over baseline, in RYGB or SG at 5 years follow-up [64].

Risk of conversion due to insufficient weight loss

Pooled results of two studies [48, 59] showed no significant differences in the risk of conversion surgery due to insufficient weight loss between SG and RYGB. See Figure 29.

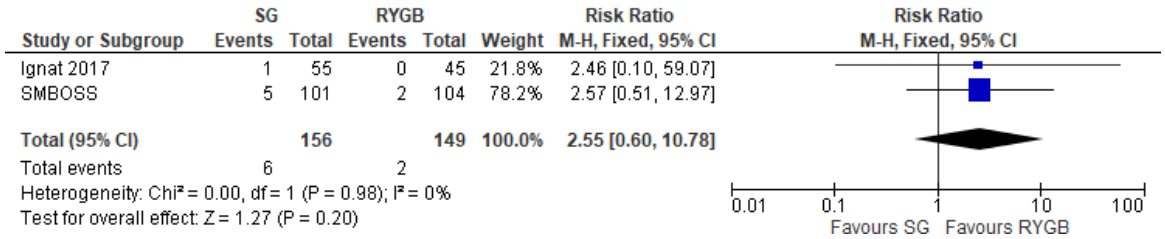


Figure 29: Risk of conversion surgery due to insufficient weight loss: SG vs. RYGB

BPD-DS vs. RYGB

One study which included participants with BMI>50 at baseline reported a similar mean weight regain from 1 to 2 years after the procedure and up to 5 years in RYGB: 9.9 kg (95% CI, 4.0 to 15.8), as in BPD-DS: 8.7 kg (95% CI, 4.8 to 12.5). There were no differences in weight regain between groups (MD: 1.7 kg (95% CI, −6.6 to 9.9; P =. 69) [32]. The weight at 5 years follow-up was significantly lower in BPD-DS as compared to RYGB (96.6 vs 119.8 kg), as was the number of participants with BMI>40 (BPD-DS: 4/29; 14.3% vs RYGB: 15/31; 55.6%).

BPD vs. RYGB

One study [53] also reported similar weight regain between years 2 and 5 in RYGB and BPD (6.09 kg [2.51] vs. 4.56 kg [5.49]) [53], and also the weight at 5 years was fairly similar in BPD and RYGB (92.8 vs. 90.3).

B-SG vs.SG

One study reported significantly lower weight regain from nadir after B-SG than after SG (5.45±6.51 vs. 10.6± 6.51%EWL) [41]. Forty-seven percent of B-SG patients reached weight nadir at last follow-up (3 years), as compared to 30% of people in the SG group.

B-RYGB vs. RYGB

One study reported a significantly smaller median weight gain 2 years from nadir in people with B-RYGB (1.1 kg) as compared to people with standard RYGB without a silicon ring (10.5 kg). More people in the RYGB group, than in the B-RYGB group, regained weight, also before 24 months [62]. The %EWL at follow-up was greater in the B-RYGB group than in the RYGB group (75.4% vs.71%).

Relapse, worsening, de novo, or unchanged obesity related comorbidity: T2D, HTN, and dyslipidemia

Four of 22 EFF studies reported on relapse, worsening, de novo or unchanged T2D, hypertension and dyslipidemia [41, 53, 59, 64].

BPD vs RYGB

One study [53], which included solely people with T2D, reported relapse of diabetes in 7/19 (36.8%) patients in the BPD group, and in 8/15 (53.3%) patients in the RYGB group at 5 years follow up.

SG vs. RYGB

One study [59] reported worsened diabetes control in 3 (11.5%) patients in the SG group and 4 (14.3%) in the RYGB group at 5 years (Absolute difference,%(95%CI): −0.05 (−0.49 to 0.48). None of the patients in the SG group experienced de novo T2D, while 3 of 76 (3.9%) patients with RYGB did (Absolute difference,% (95%CI). For three patients in the SG group (11.5%9 and 3 in the RYGB group the T2D status did not change from baseline (Absolute difference,%: 0.03 (−0.42 to 0.49). Unchanged was defined as the same symptoms and equivalent therapy; worsened as more symptoms or increase in therapy, and de novo as comorbidity not present at baseline, but newly developed within 5 years postoperatively. The same study [59] reported worsened hypertension in 4 (6.3%) patients with SG, and in 3 (4.7%) patients with RYGB at 5 years follow up (Absolute difference,% (95%CI: 0.08 (−0.38 to 0.53). The de novo cases were 2/37 (5.4%) patients

in SG and 2/40 (5.0%) in RYGB at 5 years (Absolute difference%, (95%CI: 0.01 (−0.49 to 0.51). Hypertension status was unchanged in 4 (6.3%) patients in the SG group, and in 2 (3.1) patients in RYGB (Absolute difference,% (95%CI) 0.17 (−0.30 to 0.65) at 5 years. Peterli et al [59] also reported 3/31 (9.1%) patients with SG with de novo dyslipidemia, as compared to 6/51 (11.8%) patients in the RYGB group (Absolute difference,% (95%CI: −0.07 (−0.46 to 0.32). There were no differences between groups.

One study [45] reported unchanged diabetes medication from baseline in both groups at 3 yrs (SG: 3/40; 6.5% vs. RYGB: 2/42; 4.8%), and at 5 years (SG:5/41; 12.2% vs.RYGB:2/40;5.0%).

One study [64], which included solely people with T2D, reported relapsed glycemic control in 9/18 (50%) patients with SG, and in 5/21 (24%) patients with RYGB, and diabetes relapse in 6/13 (46%) of SG patients and in 8/21 (38%) RYGB patients at 3 years follow up. At five years follow up 5/12 (41.7%) patients in the SG group and 10/20 (50%) patients in the RYGB group experienced diabetes relapse (P=0.65), 2 (4.3%) patients with SG versus 2 (4.1%) patients with RYGB experienced a >20% increase in HbA1c. For 22 (46.8%) patients with SG and for 19(38.8%) in RYGB there was no change in diabetes status from baseline. Relapse of glycemic control was defined as having met the primary end point for glycated hemoglobin of 6% or less at 1 year but not at 5 years Relapse of diabetes was defined as having met the primary end point for glycated hemoglobin of 6% or less with the use of no antidiabetic medications at 1 year but not at 5 years,

B-SG vs. SG

One study [41] reported no patients with B-SG or SG with unchanged or worsened T2DM at 3 years follow up. The same study [41] reported unchanged hypertension medication use in 1 (4.0) patient in the B-SG group, and in 2 (12.9%) patients in the SG group at 3 years follow up. None of the patients in the B-SG group had Increased blood-pressure, as compared to 1 (6.25%) patient in the SG group.

[D0011] – What is the relative effect of the different bariatric surgical procedures on cardiovascular risk (e.g. diabetes, hypertension, hyper-lipidemia)?

We could not determine the relative effect on cardiovascular risk across all procedures under study, since less than half of the included studies provided data on cardiovascular risk factors, and only single studies provided data for many of the comparisons. Results of studies comparing BPD/DS or BPD with RYGB consistently showed greater effects of BPD/DS on lipids, in people with BMI>50 (super-obesity), but little or no effect on blood pressure.

Twelve of 28 included studies (seven comparisons) provided data on complete diabetes remission which was defined as <6% HbA1c and no antidiabetic medication [6, 28, 32, 35, 37, 41, 45, 50, 53, 59, 64, 73]. Six studies (4 comparisons) provided data on blood pressure [32, 35, 37, 53, 64, 73]: at 2 years [34, 39, 69, 73], at 3 years [65], and at 5 years follow-up [39, 54, 66, 216].Eight studies (5 comparisons) provided data on remission of hypertension [32, 35, 41, 45, 51, 61, 67, 73]. Six studies provided data (5 comparisons) on lipids [32, 35, 38, 53 Svanevik, 2015 #730, 63, 73] at 2 years, and five studies provided 5 years data [39, 54, 61, 66, 216]. Four studies (1 comparison) provided data on remission of dyslipidemia [45, 51, 61, 73] at 2, 3 and 5 years follow-up. Five studies reported on severe micronutrient deficiencies that required transfusion, re-operations and/or hospital readmission [32, 35, 37, 48, 56]. No data for any of these outcomes were reported for four of the comparisons (SR-RYGB vs. RYGB; AGB vs. SG, B-RYGB vs. SG, and OAGB vs. SG).

For detailed results and definitions of complete remission used in the included studies see Table A16 – Diabetes remission, Table A21 – Lipid status, Table A17: Hypertension remission, Table A19 – Systolic blood pressure, and Table A20 – Diastolic Blood pressure.

AGB vs. RYGB

One study [37] reported no significant difference between AGB and RYGB in complete diabetes remission at 2 years follow-up, or at 5 years follow-up. The same study reported no differences in lipid status at 2 or 5 years follow-up, apart from a smaller increase in HDL in AGB at 2 years.

One study reported a greater effect on blood pressure of RYGB than of AGB at 2 years, but no difference in SBP at 5 years follow-up [39]. The same study provided no information of the use of cardiovascular drugs between groups.

BPD-DS vs RYGB

One study [32] reported no difference in complete diabetes remission, or hypertension remission between BPD-DS and RYGB at 5 years follow-up. This study included people with BMI>50 (super-obesity), of which less than 20% had T2D [32].

There was no difference in blood-pressure between BPD-DS and RYGB at 2 or 5 years follow-up. No information was provided on the use of cardiovascular drugs. The decreases in total cholesterol from BL (MD:-1.27 [-1.55, -0.99]), in LDL (MD:-0.85 [-1.18, -0.52]), and in triglycerides (MD: -0.44 [-0.76,-0.13]), were greater for BPD-DS when compared to RYGB at 5 years follow-up. The effect on HDL favoured RYGB (MD: -0.23 (-0.39; -0.07).

BPD vs. RYGB

One study [53], which included exclusively people with T2D, reported no difference in diabetes remission between BPD and RYGB at 5 years follow-up. There were no differences in blood-pressure between BPD and RYGB at 2 or 5 years follow-up. The need for CVD drugs initially decreased in both groups, and started to increase again in patients with RYGB after 2 years, while in the BPD the reduction was stable and close to zero up to up to 5 years follow-up. The decreases in total cholesterol from BL (MD:-2.30 [-3.16, -1.44]), in LDL (MD:-1.80 [-2.41, -1.19]) and in triglycerides (MD:-0.80 [-1.34,-0.26]) were greater for BPD when compared to RYGB at 5 years follow-up. The effect on HDL favoured RYGB (MD:-0.14 (-0.25; -0.03).

D-RYGB vs. RYGB

One study reported no differences in complete diabetes remission between D-RYGB and RYGB at 2 years [35]. The same study reported significantly lower hypertension remission rate after D-RYGB as compared to RYGB at 2 years (RR: 0.55 [0.35, 0.87]) [35], but no difference in blood pressure between groups (SBP: MD: -2.00 [-8.44, 4.44]; DBP: MD: 1.20 [-3.13, 5.53]). There was no difference in the number of people in each group that had stopped taking antihypertensive medication (16/20 (80%) in RYGB, and 17/25 (68%) in D-RYGB; (P =. 41). The study also reported a significantly greater effect of D-RYGB, as compared to RYGB, on all lipids but triglycerides, at 2 years follow-up [35].

OAGB vs RYGB

One study reported no differences in diabetes remission, or lipid status between OAGB and RYGB at 2 years follow-up [63].

SG vs. RYGB

Pooled results of 3 studies [45, 51, 66] showed no significant difference in diabetes remission between SG and RYGB at 3 years follow-up. Pooled results for data at 5 years follow-up [45, 59, 64] also showed no significant differences. One of the studies included people with class II obesity and T2D [64]. The other 2 studies included people with class III obesity. In the latter, the proportion of T2D was 25% [59], and 42% [45] respectively.

Pooled results of 2 studies [45, 59] showed no differences between SG and RYGB in remission of hypertension at 5 years follow-up. Heterogeneity, however, was very high for this analysis (I2=85%). In one of the studies [45] 20 of 68 patients (29%) in the SG group and 37 of 73 (51%) in the RYGB group had discontinued hypertension medications, and in the other study [64] 13 of 47 (27.6%) people with SG and 17of 49 (34.5%) with RYGB. had discontinued all CVD medication. Single studies also reported no differences in remission of hypertension at 2 years [73], or at 3 years [51]. One study showed a significant difference in BP mostly due to an increased BP in SG at 2 years (MD: 12.80 [0.17, 25.43]) [73], while one other study reported no differences at 3 or 5 years follow-up [66]. One of these studies [64] reported a similar decrease in mean number of CVD medications in both groups (RYGB: from 2.61 to 1.10, and SG: from 2.45 to 1.36) at 5 years FU.

Three studies reported no significant differences in lipid status between SG and RYGB at 2 years [73], or at 5 years follow-up [61, 66]. Pooled results of two studies showed lower dyslipidemia remission in SG as compared to RYGB at 5 years follow-up (RR: 0.72 [0.54, 0.95]) [45, 61]. See Figure 30 Results of single studies indicated no differences in dyslipidemia remission rate between RYGB and SG at 2 years [73], or at 3 years follow-up [51].

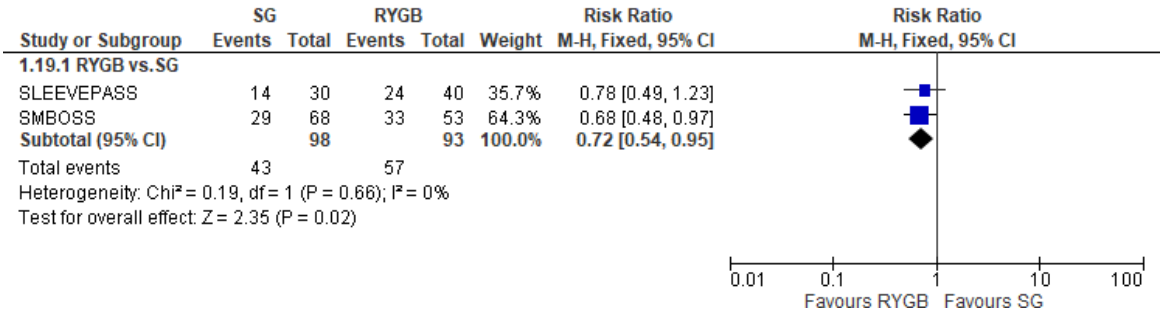


Figure 30: Dyslipidemia remission at 5 years follow-up: SG vs. RYGB

B-SG vs. SG

Cardiovascular risk

One study reported no difference in remission of hypertension between B-SG and SG at 3 years follow-up [41].

OAGB vs. SG

Cardiovascular risk

Studies do not report complete remission of diabetes. No available data on blood pressure, lipid status/remission of dyslipidemia, or micronutrient deficiencies, and unclear data on remission of hypertension [67].

Health-related quality of life

[D0012] – What is the effect of the technology on disease-specific and/or generic health-related quality of life?

[D0013] – Do the bariatric surgical procedures differ in their effect on disease-specific quality of life?

All studies reported increased health-related quality of life after obesity surgery, but little or no difference between different procedures. However, less than half of the included studies reported on quality of life, and few studies provided data for each comparison between procedures (low certainty of evidence). In addition, various QOL instruments were used to capture HRQOL. Since most studies reporting on HRQOL reported no differences between procedures, we have not presented the results for the different comparisons separately but have instead summarised the results briefly below. See Table A22 HRQOL.

Eleven of the 28 included studies reported on health related quality of life (HRQOL) at between 2 to 5 years follow-up after surgery, using one or more quality of life instruments (i.e. BAROS, SF-36/RAND-36, M-A-QoLQII, GIQLI, OWLQOL, and QOL-IWQOL) [41, 45, 48, 54, 61-63, 66, 69, 74, 216]. While all studies reported significant improvements in quality of life after surgery, eight of the 11 studies reported no differences between procedures. One study (N=94) reported greater adjusted BAROS score after B-SG, as compared to SG at 3 years [41]. One study (N=38) reported greater SF-36 scores after RYGB than after BPD-DS in three of 10 areas at 5 years follow-up [54]. One study (N= 58) reported greater QOL score in RYGB for one of eight sub-scores at 2 years, as compared to BPD-DS [34], but no differences at 5 years follow-up [216]. Note: for simplicity, only total scores are reported in the Appendix table. For details on the results of different instruments' sub-scores, the reader is referred to the original publications.

Satisfaction

[D0017] – Were patients satisfied with the technology?

We were unable to answer this research questions as none of the included studies reported on patient satisfaction with the procedure.

6 SAFETY (SAF)

6.1 Research questions

Element ID	Research question
C0008	What is the comparative safety of the different bariatric surgery procedures?
A0004	Does the frequency or severity of harms with the different bariatric surgical procedures differ depending on when (e.g. different stage of obesity), or where (e.g. low versus high volume hospitals, or private clinics) they are conducted?
A0005	Do the susceptible patient groups that are more likely to be harmed differ between the surgical procedures?
B0010	What kinds of data/records and or registry are needed to monitor the use of the different surgical procedures?

6.2 Results

Included studies

Twenty-one of the 22 effectiveness studies also reported on adverse events (AEs). An additional six studies with a follow-up of 12 months or shorter that reported on AEs were included for safety (see table 2-1). They are described briefly below [36, 40, 47, 52, 55, 58].

Country

Six additional studies with follow-up shorter than 12 months provided SAF data. Three of these studies were conducted in Europe [36, 47, 58], One originated from New Zeeland [55], one from Israel [52], and one from Egypt [40].

Populations

Three of 6 additional studies included exclusively patients with T2D [47, 52, 55].
All 3 studies included people with class 3 obesity.

Intervention and comparisons

Four studies that reported AEs only compared RYGB with SG [36, 47, 52, 58]. One study compared RYGB with OAGB [40], and 1 study compared RYGB with B-RYGB [55]. One study compared SG with B-SG [71].

Settings and experience of surgeons

All 6 additional studies reporting AEs only were single-site studies. One of these studies was described as a high-volume setting conducting between 250 to 300 RYGB and SG per year, with SG surgery accounting for approximately 10% of the total [47]. None of the other 5 studies described the setting. In 4 studies the obesity procedures were performed either by a single surgeon [52, 71], and/or by the same surgical team [58], or by the same 2 surgeons [47]. One study described the

surgeon as being an experienced bariatric surgeon and a certified specialist in gastrointestinal surgery [47]. In another study, both procedures in question (SG and B-RYGB) were described as being routine procedures at the study site [55].

Patient safety

[C0008] – What is the comparative safety of the different bariatric surgery procedures?

There is insufficient evidence to address the comparative safety across all obesity surgery procedures included in this assessment. The included studies, which reported a large number of various adverse events (AEs), used different ways of classifying and reporting these events, thereby hampering most attempts to analyse these AEs further. In addition, for many comparisons only single studies provided safety data. Some AEs however, i.e. de novo GERD, severe GERD, band problems, nutrient deficiencies, and protein malnutrition requiring admission to hospital and/or conversion surgery, are well-defined outcomes that we have included in a quantitative summary. We have presented early major and late major AEs related to the surgery in Table 20 and Table 21.

Early and late major adverse events (AEs)

Early major AEs and late major AEs requiring readmission to hospital and/or reoperation are reported in Table 20 and Table 21 respectively. This sub-set of AEs was selected after discussions with the experts involved in this REA, and constitutes:

1. Technical complications, e.g. leaks, perforations, bleedings, obstructions/strictures, internal hernias, band problems,
2. Morbidity after surgery, e.g. outcomes related to GERD, severe nutritional deficiencies requiring readmission to hospital and/or reoperation

For transparency, all AEs reported in the included studies, and details on the reporting and classification of these are listed in Table A24.

Band problems

In 4 studies of AGB, the percentage of patients experiencing band problems requiring reintervention were as follows: 9.1% [37], 16.7% [28], 17.5% [46]and 19.8% [56]

GERD

Ten studies [28, 32, 35, 41, 45, 46, 48, 50, 59, 64, 67, 74] reported on GERD symptoms after bariatric surgery. Four of these studies [41, 45, 48, 59] reported on severe GERD (2 comparisons) requiring conversion surgery. Eight studies (5 comparisons) reported symptoms of GERD after surgery [32, 41, 46, 50, 59, 64, 69, 74]. five studies reported on resolution of GERD symptoms [41, 46, 50, 59, 74], 4 studies provided data on the novo GERD after surgery [46, 59, 64, 69], and 7 studies (4 comparisons) reported severe GERD requiring conversion surgery [28, 35, 41, 45, 46, 48, 59].

See also Table A11 – Worsening of GERD; Table A12 – De Novo GERD, Table A13 – Severe GERD requiring conversion surgery and Table A14 – Resolution of GERD.

Worsening, or de novo GERD

BPD-DS vs RYGB

One study [32] reported increased GERD symptoms after BPD-DS, but not after RYGB (no numerical results provided). Five patients with RYGB (16%), and 4 patients with BPD-DS (13.8%) reported symptoms of GERD at baseline [32].

D-RYGB vs RYGB

One study reported no differences in the occurrence of GERD after RYGB and D-RYGB surgery. Symptoms of GERD were reported in 25% of people with RYGB, and in 29% of people with D-RYGB at baseline [35].

SG vs RYGB

One study reported more people experienced worsening of GERD symptoms after SG (14/44 [31.8%]), than after RYGB (vs 3/48 [6.3%]). De novo GERD was reported in 18 (31.6%) of 57 patients with SG at 5 years, but only in 6 (10.7%) of 56 of patients with RYGB [59].

One study reported symptoms of GERD in 5 of 50 (10%) people with RYGB, compared to 11 of 50 people (22%) with SG 5 years after surgery. Baseline data for GERD was not provided and it was not clear if they were de novo cases [64].

One study reported symptoms of GERD after surgery in 3/32 people with SG, and in 0/32 people with RYGB, with resolution of symptoms after 1 year [74]. Baseline data for GERD was not reported.

AGB vs SG

De novo GERD was reported in 8.8% vs. 21.8% of patients with AGB and SG respectively after 1 year, and in 20.5% vs. 3.1% of patients after 3 years [46].

Resolution of GERD

SG vs RYGB

Resolution of GERD symptoms was seen in 29 (60.4%) of 48 patients with RYGB, and in 11 (25%) of 44 of patients with SG after 5 years [59].

One study reported complete resolution of GERD in five patients after RYGB and in two patients after SG, all of whom experienced GERD before surgery [50].

One study reported that all GERD symptoms disappeared in both groups after a year [74].

AGB vs SG

One study [46] reported resolution of GERD after 1 year in 5 (83.3%) of 6 patients with AGB; and in 6 (75%) of 8 patients with SG.

B-SG vs SG

One study reported resolution of GERD in 3 (6.5%) of 7 B-SG patients, and in 4 (4.3%) of 7 SG patients after surgery. At baseline 14,6% of patients (7 in each group) reported GERD symptoms [41].

Severe GERD requiring conversion surgery

Pooled results of 3 studies [45, 48, 59] suggest a greater risk of conversion surgery due to severe GERD in SG as compared to RYGB at 5 years follow-up (RR: 12.33[2.42;62.88]. See Table 20.

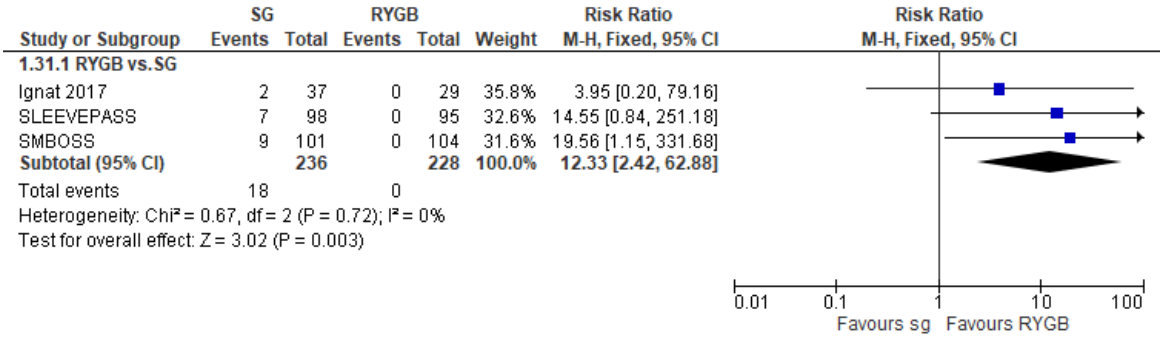


Figure 31: Conversion surgery due to severe gerd at 5 years follow-up: SG vs. RYGB

AGB vs SG or VS RYGB

One study [28] reported no significant difference in risk of conversion surgery due to severe GERD between AGB(1 of 27) and RYGB(0 of 24) at 10 years follow-up.

B-SG vs SG

Severe GERD that required conversion surgery occurred in 2 of 45 (4.4%) people with B-SG, and in 1 of 46 (2.2%) people with SG [41].

Severe micronutrient deficiencies

Six studies (5 comparisons) reported on severe micronutrient deficiencies that required transfusion, re-operations and/or hospital readmission [32, 35, 37, 48, 56, 63], see Table A15 – Micronutrient deficiencies and related morbidity.

AGB vs RYGB

Two studies reported no difference in severe iron deficiency between AGB and RYGB at 5 years follow-up (RR: 0.20 [0.02, 1.68]) [37], and also no differences at 10 years. Neither study described supplementation after surgery.

BPD/DS vs RYGB

One study [32] reported no significant differences in severe iron deficiency between RYGB (1/31; 3.2%), and BPD-DS (5/29; 17.2%) at 5 years follow-up (RR: 5.34 [0.66, 43.06]).

The same study also reported no difference in severe protein-caloric malnutrition requiring hospitalisation between BPD-DS (4/29; 13.8%), and RYGB (0/31; 0%) at 5 years (RR: 9.60 [0.54, 170.84]). In addition, 2 cases of night blindness due to severe vitamin A deficiency were detected in the BPD-DS group, but no cases in RYGB [32]. The CIs, in these analyses, however, all included both the point of no effect and the possibility of a greatly increased risk of both iron deficiency and protein-caloric malnutrition in BPD-DS. Prescription for both groups was a standard regimen of vitamin and mineral supplementation after surgery.

D-RYGB vs RYGB

One study [35] reported no significant difference in severe iron deficiency in people with D-RYGB (3/56; 5.3%), as compared to RYGB (0/57) at 2 years follow-up (RR: 7.12 [0.38, 134.81]).

The same study reported severe protein-calorie malnutrition in 3 of 56 patients in the D-RYGB arm, and severe vitamin deficiency also in 3 people, but no cases among patients in the RYGB group (RR: 7.12 [0.38, 134.81]) [35]. The CIs for both outcomes included both the point of no effect but also the possibility of a much larger risk of deficiencies in the D-RYGB group. Three patients in the D-RYGB group, with multiple deficiencies, required revision surgery with elongation of the common channel to reduce malabsorption [35]. It was recommended that all patients take a standard daily oral supplement of a multivitamin and mineral tablet, iron, calcium, and vitamin D. Vitamin B12 was administered through injections.

OAGB vs RYGB

One study [63] reported no difference in severe iron deficiency between people with OAGB (1/86; 1.2%), and people with RYGB (0/91) at 2 years follow-up (RR: 2.63 [0.11, 63.15]], but there was a significantly greater risk of other complications for OAGB (RR: 20.09 [1.19, 340.01]). Two of these complications required conversion surgery. All complications, i.e. feeding difficulties (1), anorexia (1), food intolerance (1), and diarrhoea/malnutrition (4), required admission to hospital. All patients were prescribed supplementation of multivitamins, iron, calcium, vitamin B12, and vitamin D.

RYGB vs SG

One study [48] reported no significant difference in the occurrence of anemia requiring hospital admission between RYGB (7/45; 15.5%), and SG (2/55; 3.6%) at 5 years follow-up (RR: 0.23 [0.05, 1.07]. No information was provided regarding any supplementation after surgery.

ADVERSE EFFECTS ON BONE HEALTH

Three studies reported morbidity secondary to nutritional deficiencies: i.e. osteopenia [32, 53], osteoporosis [32], and bone fractures [32, 37, 64].

AGB vs RYGB

Results of one study [37] indicate that bone fractures may be more frequent in RYGB (2/16;12.5%) than in AGB (0/20) at 5 years follow-up.

SG vs RYGB

One study [64] reported 4 limb fractures in 50 (8%) RYGB patients, and 6 fractures in 49 people with SG (12.2%) at 5 years follow-up. It was not clear, however, whether these fractures were due to poor bone health.

BPD-DS vs RYGB

One study [32] reported no significant difference in the occurrence of osteopenia or osteoporosis between BPD/DS and RYGB (RR: 3.20 [0.14:75.55]) at 5 years follow-up [32].

In addition [32] traumatic bone fractures was reported in two of 29 (6.9%) BPD/DS patients, and no fractures in 31 people with RYGB [32]. It was however not clear if these fractures were due to poor bone health.

BPD vs RYGB

One study [53] reported no difference in bone health outcomes between BPD and RYGB at 5 years follow-up (RR: 5.00 [0.26; 97.70]. There was great uncertainty related to these results as the CI covered the point of no effect but also the possibility of a large negative effect of both BPD/DS and BPD on bone health.

Readmissions and/or reoperations

Re-operations and hospital re-admissions may be the results of adverse events occurring after the surgery, but they may also be unrelated to the initial surgery. Readmissions and reoperations (as well as length of stay) are considered as resource use. Seventeen of the 27 included trials reported on early and late 'reoperations' after obesity surgery. See Table 20 and Table 21.

This outcome was defined as 'any reoperation' in some studies, 'reoperations related to the initial surgery' in some, while yet other studies reported a composite outcome of re-operations and re-admissions. The different ways of reporting this outcome hampered any attempt to analyse this data in a meaningful way. More well-defined types of reoperations i.e. conversion surgery due to severe GERD, or re-operations due to insufficient weight loss are reported above. For the outcome re-admissions, the problem was basically the same, with some studies reporting 'readmissions related to the initial surgery', some reporting 'any readmissions', and yet others reporting a composite outcome of 'any readmission or reintervention'.

RESOURCE USE

Length of hospital stay

Twelve of the included trials reported one or more measure of hospital length of stay (LoS). Most often reported was the mean (or median) LoS of the initial procedure [28, 30, 35, 42, 47, 48, 56, 58, 63, 67, 71, 73]. Few studies reported the LoS for early or late readmissions due to complications [28, 48, 71], and even fewer reported on the need for ICU stay [28, 56]. Mean LoS for the different procedures ranged from 1.5 [56] to 2 days [28] for AGB, from 2.5 days [73] to 7 days [30] for RYGB, from 3.0 [73] to 3.9 days for SG [67], One study of BPD-DS reported a LOS of 7.7 days [42]. See Table A23 – Hospital length of stay.

[C0004] – Does the frequency or severity of harms with the different bariatric surgical procedures differ depending on when (e.g. different stage of obesity), or where (e.g. low versus high volume hospitals, or private clinics) they are conducted?

We cannot answer this question. Few of the included studies provided information on the annual volume of bariatric surgery procedures, the experience of the participating surgeons, or the type of participating hospitals or clinics (public or private) that constituted the study sites.

[C0005] – Do the susceptible patient groups that are more likely to be harmed differ between the surgical procedures?

We cannot answer this question as none of the included studies addressed the possibility of differential effects of bariatric surgery procedures on different groups of people. In addition, it is not clear which patient groups would be considered susceptible to harm from the surgery.

[B0010] – What kinds of data/records and or registry are needed to monitor the use of the different surgical procedures?

In Norway, as well as in other countries (e.g. Sweden), obesity surgery registries are in current use [217]. Registries can be used to ensure that the most effective and safest procedures are identified and selected to be used by health professionals, and that patients, irrespective of where they live, are offered the best available care/treatment. Registries may be used to tailor treatments/procedures to specific patient groups with and without comorbidities. They can also be used as benchmarking tools, allowing health professionals to compare the results at their own clinic with results at a National level for improved quality. Thus, registries can potentially play an important role in improving health outcomes. In summary, using registries could be a way of decreasing the variance in practice and an opportunity to improve practice.

Table 20: Early major (serious) adverse events (<30 days after procedure) requiring readmission/reoperation

Author, year	Arm	Number of pts	Re-operations (excl. endoscopy-radiology)	Hospital readmissions	Leaks, perforations, and occlusions	Bleedings that require reop. or transfusions	Stenoses strictures, obstructions, internal hernias (fistulas)	Deep thromboses and embolisms	MI/stroke	GERD and severe dysphagia	Band problems (e.g. slippage, erosion)
AGB vs. RYGB											
Angrisani 2007 [28]	AGB	30	0		0						
	RYGB	29	2		2						
Courcoulas [§] [‡] 2014/TRIABETES [37]	AGB	60	1								
	RYGB	60	0								
Nguyen 2009, 2018 [56, 57]	AGB	86	1	0		0	1				
	RYGB	111	6	6		2	5				
AGB vs. SG											
Himpens 2006 [§] [46]	AGB	40	0			0					
	SG	40	2			1					
SG vs. RYGB											
Hofsø 2019 [‡] [§§] OSEBERG [47]	SG	55			0	1					
	RYGB	54			1	0					
Ignat 2017 [48]	SG	55				0					
	RYGB	45				1					
Karamanakos 2008 [50]	SG	30	1		1		1				
	RYGB	30	2		0		2				
Paluszkiewicz 2012 [58]	SG	36	2	0		1	1				
	RYGB	36	0	0		0	0				
Peterli 2014 SMBOSS [59]	SG	107	1		0	0	1				
	RYGB	110	9		1	1[c]	1				
Shauer 2012 [§] [‡] STAMPEDE [64]	SG	50	1	4							
	RYGB	50	3	11							
Salminen 2018 SLEEVEPASS [45]	SG	121	3		1	3	1				
	RYGB	119	4		0	7[f]	0				
Wallenius 2020 [‡] CONTROL [73]	SG	24	1[e]		1	1	0				
	RYGB	25	1		1	0	1				
Zhang 2014 [§] [74]	SG	32	0		0	1				3	
	RYGB	32	1		1	1				0	
D-RYGB vs RYGB											
Svanevik 2015 [†] [§§] [35]	D-RYGB	62	6		2	1	3				
	RYGB	61	0		0	0	0				

Author, year	**Arm**	**Number of pts**	**Re-operations** (excl. endoscopy-radiology)	**Hospital readmissions**	**Leaks, perforations, and occlusions**	**Bleedings that require reop. or transfusions**	**Stenoses strictures, obstructions, internal hernias** (fistulas)	**Deep thromboses and embolisms**	**MI/stroke**	**GERD** and severe dysphagia	**Band problems** (e.g. slippage, erosion)
OAGB vs. RYGB											
Robert 2019 [§§] YOMEGA [63]	OAGB	129	1		0					3	
	RYGB	124	2		1					0	
Seethamaraiha 2017 [67]	OAGB	109	0	10	0	2				2	
	SG	108	1	12	1	1				3	
BPD-DS vs. RYGB											
Aasheim 2009 [†] [§§] [32]	BPD-DS	29	1	4	2		1				
	RYGB	31	2	6	2		0				
Hedberg 2012 [†] [c] [42]	BPD-DS	24	2					1			
	RYGB	23	1					0			
BPD vs RYGB											
Mingrone 2012 [‡] DIABASY (NR) [53]	BPD	20									
	RYGB	20									
Combined (banded) procedures vs. standard procedure or other procedure											
Arceo Olaiz 2008 [30]	B-RYGB	30			1		1				1
	RYGB	30			1[a]		1[b]				NA
Murphy 2018 [‡] (NR) [55]	B-RYGB	58									
	SG	56									
Rasera 2015 (NR) [62]	B-RYGB	200									
	RYGB	200									
Fink 2020/MISO [†] (No AEs) [41]	B-SG	47									
	SG	47									
Tognoni 2016 [71]	B-SG	25	0			1	0				
	SG	25	1[d]			1	1				

[†] Super-obesity (BMI>50); [§]Class 2 obesity (BMI>30); [‡] T2DM population; [§§] High volume hospitals/clinics;

[a] The leaks did not result in reoperation in either group, [b] Internal hernias that resulted in obstructions in both groups;
[c] did not require reoperation; [d] one conversion; [e] one conversion; [f] unclear if re-operation was needed;
Studies not reporting on early AEs: Biter 2020; Keidar 2013[‡]; Capristo 2018; Fahmy 2018;

Table 21: Late major (serious) AEs (>30 d after procedure) requiring readmission/reoperation

Author, year	Arm	No of pts.	Re-operations (excl. endoscopy-radiology)	Re-operation due to inefficacy	Hospital re-admission	Leaks, perforations, occlusions	Bleedings that require re-op. or transfusions	Stenoses, strictures, obstructions, internal hernias, (fistulas)	MI/stroke	GERD and severe dysphagia	Band problems (e.g. slippage, erosion)	Nutritional deficiencies requiring readmission
AGB vs. RYGB												
Angrisani 2007 [28]	AGB	30	9	4				0		1	5	
	RYGB	29	4	0				2		0	NA	
Courcoulas § ‡ 2012 TRIABETES [37]	AGB	22	1	1	3	0					2	0
	RYGB	24	1	1[e]	1	1					NA	1[f]
Nguyen 2009 [56]	AGB	86	20	5		0		0			17	0
	RYGB	111	3	0				3			NA	4[i]
AGB vs. SG												
Himpens 2006 § [46]	AGB	40	7	2						3	7	
	SG	40	0	2						7	NA	
SG vs. RYGB												
Biter 2020 [19]	SG	315										
	RYGB	308										
Capristo 2018 [36]	SG	60			0							
	RYGB	60			4[d]							
Hofsø 2011 ‡ §§ OSEBERG [47]	SG	55			5							
	RYGB	54			7							
Ignat 2017 [48]	SG	55	2	1	10	0		0		2		2
	RYGB	45	7[g]	0	21	2		1		0		7[h]
Karamanakos 2008 [50]	SG	30	1			1		0				
	RYGB	30	0			0		1				
Keidar 2013 ‡ (NR) [52]	SG	19										
	RYGB	22										
Paluszkiewicz 2012 [58]	SG	36						0				
	RYGB	36						1				
Peterli 2014 SMBOSS [59]	SG	107	23	2				0		9[k]		
	RYGB	110	16[j]	5				2		0		
Salminen 2018 SLEEVEPASS [45]	SG	121	10					0		7		
	RYGB	119	18[n]					17		0		
Schauer 2012 § ‡ STAMPEDE [64]	SG	50	1		4	1	0	0	1	13		
	RYGB	50	3[o]		11	0	2	5	0	5		
Wallenius 2020 ‡ CONTROL (NR) [73]	SG	24										
	RYGB	25										
Zhang 2014 § [74]	SG	32	0					0		3		
	RYGB	32	1					3		0		

Author, year	Arm	No of pts.	Re-operations (excl. endoscopy-radiology)	Re-operation due to inefficacy	Hospital re-admission	Leaks, perforations, occlusions	Bleedings that require re-op. or transfusions	Stenoses, strictures, obstructions, internal hernias, (fistulas)	MI/stroke	GERD and severe dysphagia	Band problems (e.g. slippage, erosion)	Nutritional deficiencies requiring readmission
D-RYGB vs. RYGB												
Svanevik 2015 † §§ [35]	D-RYGB	62	4		17			3				9[p]
	RYGB	61	11		30[o]			7				1
BPD-DS vs. RYGB												
Aasheim 2009 † §§ [32]	BPD-DS	29	14	14	17/40	1		2				5+4
	RYGB	31	4[a]	0	9/16[b]	1		2				1+0[c]
Hedberg 2012 † [42]	BPD-DS	24			4			3				
	RYGB	23			3			2				
BPD vs. RYGB												
Mingrone 2012 ‡ DIBASY [53]	BPD-BS	20	1					1				
	RYGB	20	1					1				
OAGB vs. RYGB												
Fahmy 2018 [40]	OAGB	30						o				
	RYGB	30						2				
Robert 2019 §§ YOMEGA [63]	OAGB	129	4 [l]				0	1		3		9[m]
	RYGB	124	NR				0	3		0		0
OAGB vs. SG												
Seethamariah 2017 [67]	OAGB	109		0	12				0			
	SG	108		1	13				1			
Combined procedures vs. standard or other procedure												
Arceo-Olfaiz [30]	B-RYGB	30	1								1	
	RYGB	30									NA	
Murphy 2018 ‡ [55]	B-RYGB	58	5			2	1	0			1	
	SG	56	3			0	0	1			NA	
Rasera 2015 [62]	B-RYGB	200	2					5				
	RYGB	200	2					2				
Fink 2020 † MISO [41]	B-SG	47	3					0		2	1	
	SG	47	1					1		1	NA	
Tognoni 2016 [71]	B-SG	25										
	SG	25										

† Super-obesity (BMI>50); § Class 2 obesity (BMI>30); ‡ T2DM population; §§ High volume hospitals/clinics; Biter 2020 did not report on AEs.

[a] Surgery related to the initial bariatric procedure reported; [b] Number of patients with hospital admissions/number of total hospital admissions: [c] Number of patients with iron deficiency requiring blood transfusion, [+] no of patients with protein-calorie deficiency requiring hospitalization; [d] Four of 59 RYGB subjects (6.8%) had 1 to 3 hospitalizations for symptomatic hypoglycemia vs 0 in SG: [e] described as bariatric re-operation, but not completely clear if due to inefficiency: [f] Severe iron deficiency; [g] Reoperation or readmission; [h] Severe iron deficiency; [i] severe iron deficiency; [j] reop or re-intervention; [k] 9 conversions; [l] conversions to RYGB; [m] Nutritional deficiencies: 3 protein-calorie malnutrition, 3 anemia, 3 severe vitamin deficiency; [n] re-operations or readmissions; [o] any readmission; [p] nutritional complications: Wernicke's encephalopathy(1), feeding difficulties (1), anorexia (1), food intolerance (1), and diarrhea/malnutrition (5)

Table 22: Early deaths across included studies and procedures

Author, year	FU, yrs	RYGB	SG	OAGB	AGB	B-RYGB	D-RYGB	BPD-DS	BPD	B-SG	Cause	Timing
Aasheim 2009 [32]	5	0/31						0/29				
Angrisani 2007 [28]	10	0/29			0/30							
Arceo-Olfaiz 2008[2] [30]	5	0/30				0/30						
Biter 2020 (NR) [19]	2	-	-									
Capristo 2018 [36]	1	0/60	0/60									
Courcoulas 2020-TRIABETES [37]	5	0/24			0/22							
Fahmy 2018 [40]	1	0/30		0/30								
Fink 2020-MISO [41]	3		0/47							0/47		
Hedberg 2012 [42]	3	0/23						**1/24**			pulmonary embolism	3 weeks
Himpens 2006 [46]	3		0/40		0/40							
Hofsø 2019-OSEBERG [47]	1	0/54	0/55									
Ignat 2017 (NR) [48]	5	-	-									
Karamanakos 2009 [50]	3	0/30	0/30									
Keidar 2013 [52]	1	0/22	0/19									
Mingrone 2012DIBASY [53]	5	0/20							0/20			
Murphy 2019 [55]	1	0/56	0/58									
Nguyen 2009 [56]	10	0/111			0/86							
Rasera 2015[2] [62]	2	**1/200**				**1/200**					Infections, and multiple organ failure	NR (assumed early)
Robert 2019-YOMEGA [63]	2	0/129		0/124								
Paluszkiewicz 2012 [58]	1	0/36	0/36									
Peterli 2014SMBOSS [59]	5	**1/110**	0/107								surgery complications	< 30 d
Salminen 2018-SLEEVEPASS [45]	5	0/119	0/121									
Schauer 2012- STAMPEDE [64]	5	0/50	0/50									

Author, year	FU, yrs	RYGB	SG	OAGB	AGB	B-RYGB	D-RYGB	BPD-DS	BPD	B-SG	Cause	Timing
Seethamariah 2017 [67]	3		0/100	0/101								
Svanevik 2015 [35]	5	0/57					0/56					
Tognoni 2013 [71]	4		0/25							0/25		
Wallenius 2020-CONTROL [73]	2	0/29	0/31									
Zhang 2014 [74]	5	0/32	0/32									
Total no of early deaths per procedure		2	0	0	0	1	0	1	0	0		
Total no of pts		**1,341**	**811**	**285**	**178**	**230**	**56**	**53**	**20**	**72**		

[1] Unclear in which group the death due to melanoma occurred. [2] Unclear in which group the three unrelated deaths occurred, RYGB: Roux -en-Y gastric bypass (SR-RYGB: RYGB with silicon ring; D-RYGB: distal RYGB); SG: sleeve gastrectomy (B-SG: banded SG); OAGB: One Anastomosis Gastric Bypass; AGB: Adjustable Gastric Banding; BPD: Bileopancreatic Diversion; BPD-DS: Bileo Pancreatic Diversion with Duodenal Switch; DS: Duodenal Switch

Table 23: Late deaths across included studies and procedures

Author year	FU, yrs	RYGB	SG	OAGB	AGB	B-RYGB	D-RYGB	BPD-DS	BPD	B-SG	Reason for death	Timing
Aasheim 2009 [32]	5	**1/31**						0/29			Cancer (renal)	4 years
Angrisani 2007 [28]	10	0/29			0/30							
Arceo-Olfaiz 2008[2] [30]	5	**?/30**				?/30					Cancer (one melanoma)	3 years
Biter 2020 (NR) [19]	2	-	-									
Capristo 2018 [36]	1	0/60	0/60									
Courcoulas 2020-TRIABETES [37]	5	0/24			0/22							
Fahmy 2018 [40]	1	0/30		0/30								
Fink 2020-MISO [41]	3		0/47							0/47		
Hedberg 2012 [42]	3	0/23						0/24				
Himpens 2006 [46]	3		0/40		0/40							
Hofsø 2019-OSEBERG [47]	1	0/54	0/55									
Ignat 2017 (NR) [48]	5	-	-									

Author year	FU, yrs	RYGB	SG	OAGB	AGB	B-RYGB	D-RYGB	BPD-DS	BPD	B-SG	Reason for death	Timing
Karamanakos 2009 [50]	3	0/30	0/30									
Keidar 2013 [52]	1	0/22	0/19									
Mingrone 2012DIBASY [53]	5	0/20							0/20			
Murphy 2019 [55]	1	0/56	0/58									
Nguyen 2009 [56]	10	**2/111**			0/86						Alcohol-related deaths	NR
Rasera 2015[2] [62]	2	**1/200**				**2/200**					Cholelithiasis (2), sudden death (1); unrelated to surgery	at 19 -24 months
Robert 2019-YOMEGA [63]	2	0/129		**2/124**							NR, may be early or late	NR
Paluszkiewicz 2012 [58]	1	0/36	0/36									
Peterli 2014SMBOSS [59]	5	**1/110**	0/107								Cancer (lymphoma)	(i) at < 30 d; (ii) at 2,5 yrs
Salminen 2018-SLEEVEPASS [45]	5	**2/119**	**2/121**								NR; unrelated to surgery	NR
Schauer 2012- STAMPEDE [64]	5	0/50	0/50									
Seethamariah 2017 [67]	3		**1/100**	**1/101**							(i) SG: MI; (ii) OAGB: NR	(i)1 yrs; (ii) 2 yrs
Svanevik 2015 [35]	5	0/57					0/56					
Tognoni 2013 [71]	4		0/25							0/25		
Wallenius 2020-CONTROL [73]	2	0/29	0/31									
Zhang 2014 [74]	5	0/32	0/32									
Total no of late deaths		7	3	3	0	2	0	0	0	0		
No of person years		4,898	2,591	581	1,390	550	280	217	100	241		
No of late deaths per 10,000 person-years		14,0	11,6	51,6	-	36.4	-	-	-	-		
Total no of pts		**1,341**	**811**	**285**	**178**	**230**	**56**	**53**	**20**	**72**		

[1] Unclear in which group the melanoma occurred. [2] Unclear in which group the three unrelated deaths occurred, RYGB: Roux -en-Y gastric bypass (SR-RYGB: RYGB with silicon ring; D-RYGB: distal RYGB); SG: sleeve gastrectomy (B-SG: banded SG); OAGB: One Anastomosis Gastric Bypass; AGB: Adjustable Gastric Banding; BPD: Bileopancreatic Diversion; BPD-DS: Bileopancreatic Diversion with Duodenal Switch; DS: Duodenal Switch

7 DISCUSSION

The aim of this REA, which included network meta-analysis (NMA) methods, was to determine the comparative effectiveness (and potential superiority) of different types of bariatric procedures in improving important outcomes for adults with obesity, e.g. weight loss and diabetes control.

The assessment included 28 trials, reported in 70 studies (11 comparisons), involving seven surgical procedures for the treatment of obesity (AGB, SG, RYGB, OAGB, BPD-DS, BPD), and two combined procedures involving rings or bandings (B-RYGB and B-SG). Twenty-two of the 28 studies provided EFF data. Twenty-one of these, and an additional 6 studies with shorter follow-up provided data for the SAF domain. The total number of participants included in these trials was 3,799. Four studies included people with class II obesity [37, 46, 64, 74] The remaining studies included people with class III obesity, of which 4 studies included people with a BMI>50 (super-obesity) [32, 35, 41, 42]. Four EFF studies [37, 53, 64, 73], and three SAF studies [47, 52, 55] included exclusively people with T2D. The proportion of people with T2D, and other co-morbidities, varied greatly across the other included studies. For 5 of the comparisons (5 procedures) only evidence from single studies was available. Randomised evidence for the effectiveness of SASI or SADI-S was not available. The median follow-up time for the included EFF studies was 4 years (range: 2 to 10), and only 2 studies reported long-term follow-up (>5 yrs).

This assessment provides up-to-date evidence, including studies with longer follow-up than other recent systematic reviews with NMAs on weight [218] and diabetes control outcomes after bariatric surgery [219].

Interpretation of the findings

Effectiveness

Weight loss and diabetes status

The results of the NMAs suggest little or no difference in the effects on weight loss and diabetes status between procedures at 2 years follow-up (low to very low certainty of evidence), as well as for weight outcomes at 3 years follow-up (low to very low certainty of evidence).

Our results of no difference in weight loss between SG and RYGB are in accordance with another SR and NMA [218], which included RCTs of SG, RYGB and AGB procedures only. On the other hand, the results of Kang et al suggest a superiority of both SG and RYGB over AGB which we did not find in our NMA. In Kang et al. however [218], almost 50% of included studies had short follow-up (1 year), and were thus not included in our review. However, almost 50% of included studies had short follow-up (1 year), and were thus not included in our review. In addition, all studies in Kang's review were published before 2014, while our review includes more up-to-date evidence both for the comparison of SG vs RYGB (7 new studies), and for AGB vs. RYGB (3 studies with longer follow-up) [28, 37, 56]. No new randomised evidence comparing SG with AGB has emerged since the publication of the Kang's review, and thus only a single RCT provided evidence for SG vs AGB in our review as well. Kang's review reported solely on weight outcomes. Another difference is that Kang et al. performed separate analyses of BMI change and% EWL while these outcomes were combined in our analyses, which may also have affected the differences between our results for RYGB and AGB. However, while our NMA showed no superiority of RYGB, two studies with 10 years follow-up (not included in the NMA) both reported superior effects of RYGB on weight loss as compared to AGB.

The NMAs of diabetes outcomes did not reveal any differences between SG and RYGB in our review, which is in accordance with another SR and NMA of RCTs on the topic [219]. Kodama et al. included six bariatric procedures that were reported in six studies (of a total of 25 included studies) that were eligible for inclusion also in our review, while the other studies did not match our inclusion criteria (i.e. comparisons with non-surgical treatment, ineligible BMI, or short term follow-up). The Kodama review [219] suggests greater diabetes remission for patients with BPD-DS (and OAGB) than for RYGB patients. This is partly similar to our results of superiority of BPD-DS to RYGBat 2 years (but not at 3 years), and of OAGB also showing superiority to RYGB at 2 years and to D-RYGB at 5 years, but results were mostly inconsistent across analyses with fixed and random effect models. Three of the studies concerning BPD and/or BPD-DS included in the Kodama review were also included in our review, while one non-randomised study included by Kodama, was not. A review by Park et al [220] reported similar %EWL of SG, RYGB, and BPD-DS up to 3 years, but longer follow-up was not available. However, since few studies compared BPD-DS, BPD, OAGB and D-RYGB with RYGB, these results should be interpreted with caution.

We found little differences in weight regain between procedures, and only single studies that compared B-SG and B-RYGB to the standard procedures without banding, reported less weight gain for the banded procedures. Pooled results (2 studies) suggest more than 11 times higher risk of conversion surgery due to insufficient weight loss in AGB as compared to RYGB at 5 years follow-up. Band problems such as slippage and ulcerations, requiring reoperation, were also common (from 9.1%-19.8% across studies). Our findings of greater risk of reoperations in AGB are in accordance with results for AGB reported in a recently published bariatric surgery guideline [4].

Cardiovascular disease risk reduction

Pooled results of 2 trials suggest poorer remission of dyslipidemia in patients with SG as compared to patients with RYGB and no difference in lipid status, but mixed results for remission of hypertension. Our results contradict the summarised results reported in a recent guideline [4], suggesting greater remission of hypertension and dyslipidemia in SG as compared to RYGB. These results, however, are based on evidence from observational studies, while our results on hypertension were based on four RCTs with 2-5 years follow-up. Longer follow-up was lacking for cardiovascular risk reduction after BS.

Single studies consistently reported superior effects of the more malabsorptive bariatric procedures (BPD-DS, BPD and D-RYGB) on many cardiovascular risk factors (total cholesterol, LDL and triglycerides), and mixed results for diabetes remission (dichotomous outcome) as compared to RYGB at 5 years follow-up.

Contrary to our findings of no clear superior effect of BPD-DS on diabetes remission, Kodama et al. [219] reported a higher probability for diabetes remission for BPD (without DS) and OAGB, than for other treatments. They exclusively considered diabetes remission outcomes. Kodama et al also included non-surgical treatments and combined all follow-up times in a single analysis. They limited inclusion of studies to a maximum HbA1c of 6.5% and/or fasting plasma glucose of 7.00 mmol L-1 without hypoglycemic agents were used as a cut-off for diabetes remission, all of which may have contributed to our different results.

Health-related Quality of Life

Even though improved health-related quality of life (HRQOL) after bariatric surgery is an outcome of great importance to patients, only 11 of the 28 studies included in this assessment reported on HRQOL. The overall effect across all procedures was improved quality of life after surgery, which

is in agreement with results from a systematic review of HRQOL in bariatric surgery [221]. The relative effect of different procedures on HRQOL could not be assessed quantitatively but results across individual studies and comparisons suggest little or no difference between procedures (low certainty of evidence). The results of no difference in quality of life between SG and RYGB (4 studies reporting) is a bit surprising due to potentially greater problems with GERD in SG patients, however GERD was not specifically explored in these studies.

Safety of bariatric surgery

Mortality

Based on the available information in this review, it is not possible to say whether the risk of early death (or late death) differ between bariatric procedures, or if other factors are more important for determining short- or long-term mortality. There were four early deaths (in 3 studies) due to complications after surgery in a total of 3,799 participants (0.11%), which is similar to results from a systematic review of 0.18% early deaths (38 RCTs in analysis) after bariatric surgery [222]. It was not possible to determine whether the early deaths (2 RYGB, and 1 B-RYGB) caused by surgical complications were correlated to annual hospital volume, the experience of surgeons, or the status of the participating hospitals/clinics (i.e. private or public), as this information was not provided in all studies. No information on the annual hospital volume or the experience of surgeons were provided in 2 of the studies, and in the third study which had been conducted in high volume settings with experienced surgeons, it was unclear whether the bariatric clinics that took part in this study were private or public [59]. The one death after BPD-DS that occurred in a study of people with BMI>50 (super-obesity), was due to a lung embolus. A possible contributing factor to this death may be the very high BMI of the participant, as greater BMI may result in longer operation times, which in turn may increase the risk of lung emboli [223]. In the study in question, the operation time for BPD-DS was significantly longer than that of RYGB [42]. It should be noted that since these results are based solely on data from RCTs, which may be affected by learning curve aspects for experimental procedures and inclusion of selected patient categories (e.g. patients with extra high BMI, type 2 diabetes etc.), results of larger pragmatic, everyday observational studies may deviate from our findings

GERD

While the results of the NMAs suggest little to no differences in the effects on weight-related outcomes and diabetes control between SG and RYGB, pooled results suggest 12 times greater risk of severe GERD requiring conversion surgery for patients with SG, as compared to patients with RYGB. Results from pooled analysis of the novo cases also support a potentially greater risk of SG, as compared to RYGB. Un-pooled data also suggest poorer resolution of GERD in SG, as compared to RYGB. Our findings are in concordance with the results of increased de novo GERD after SG reported in a recently published guideline [4], but do not support the increased resolution of GERD in patients with SG reported in the same guideline. A general problem of the evidence is the subjectivity concerning what actually constitutes a worsening condition, and that in some cases, it was not absolutely clear whether reported cases were de novo, or cases that existed before surgery. Sometimes there were no baseline data. Again, for this outcome as well, there is a lack of randomised long-term data. The results from a large register study suggesting improved resolution of GERD after RYGB as compared to SG [224] also support our finding.

Micronutrient deficiencies and related morbidity

Un-pooled results (single studies) of safety after BPD- DS, and OAGB, suggest an overall greater number of micronutrient deficiencies, metabolic complications, and serious adverse events for these procedures, as compared to RYGB. For most analyses the CI included the point of no effect, but also the possibility of a much larger risk of adverse events for BPD-DS and OAGB, than for RYGB. However, 1 of the studies [63], which reported more than 20 times greater risk of metabolic complications after OAGB, as compared to RYGB, suffered from large losses to follow-up. Two studies comparing AGB with RYGB showed little to no difference in micronutrient status between groups. Studies with long-term follow-up are lacking.

Fractures

Increased risk of poor bone health and fractures has been documented, for example, in the Swedish SOS cohort study [225], which includes a number of selected bariatric procedures and a follow-up time of 26 years. The cohort, however, does not cover all bariatric surgery procedures included in our review. Only a few of our included studies reported on outcomes related to bone health (osteoporosis, osteopenia and fractures). Few events were documented (after BPD, RYGB, and SG), and of the results were not convincing for any of the comparisons. Controlled cohort studies with longer follow-up, and the use of bariatric surgery registers are probably better suited to address this important issue.

Limitations with the available data

Quality of the evidence, lack of long term follow-up, heterogeneity in reporting

A majority of the included RCTs were at high risk of bias. Only a handful of RCTs provided high quality evidence, mainly for the comparison of SG vs. RYGB. There was a lack of studies with long-term follow-up (>5 years). The limited availability of long-term follow-up data is a major limitation in the literature at the present time. Nevertheless, this work represents a synthesis of the highest quality evidence. Updates to this systematic review will be necessary as long-term evidence becomes available.

The selection of only RCTs is another potential limitation, and it may be argued that well-performed cohort studies with longer follow-up could have provided valuable evidence for our research questions. However, allocation of participants to groups in non-randomised studies is typically based on patient preference, clinical decision-making, and shared clinical decison-making. Therefore, results from non-randomised studies may be biased because the characteristics of populations selected for a particular procedure may differ, limiting the usefulness of this evidence, in particular in the evaluation of head-to-head comparisons.

Heterogeneity in reporting, multiple comparisons, and great variations in comorbidities across included studies makes evaluations and interpretations of findings challenging. Definitions of comorbidity resolution, improvement or relapse/worsening, and adverse event classification (late and early complications; major and minor complications; SAEs only) were heterogenous across studies which presents challenges for comparison of results. This highlights the need for adopting standardised definitions for incorporation into core outcome sets to facilitate consistent reporting.

Available diabetes data for NMA and dichotomous analysis

Another limitation, related to the available diabetes data for the NMAs, was that not all studies reported HbA1c outcomes, which according to experts constitute a reliable measure of diabetes status, even though not perfect under all conditions [226]. Moreover, the data included in the SMD calculations were based on a ranked sequence of continuous diabetes outcomes (for details see p. 27-28), but did not take into consideration reduced or discontinued use of antidiabetic drugs when describing diabetes control. Using continuous diabetes data enabled us to include more studies in the analysis. However, in the analysis of dichotomous outcomes, both target HbA1c and stopped antidiabetic medication were taken into account, but not all studies reported on diabetes remission. As the proportion of T2D patients varied greatly across studies, and only four EFF studies included solely T2D patients, diabetes remission was probably not the focus in these studies, which may explain the non-reporting.

Varying co-morbidity profiles

The varying comorbidity profiles across included studies is another limitation for the comparison between studies, as this may have an effect on the response to the intervention. Some studies in our review included only people with T2D, one study excluded diabetics, and for the other co-morbidities (e.g. hypertension, dyslipidemia) the number of people affected varied greatly across included studies.

Safety evidence only from RCTs

Our assessment is limited to RCTs addressing safety, which is a major limitation in this important work, especially since the included RCTs had a limited follow-up. There is a rising concern for GERD after SG, for which long-term observations is of great importance [227]. By not including non-randomised evidence on adverse events we may have missed robust longitudinal studies with longer follow-up that could have added to the body of evidence in particular pertaining to the safety outcomes. We are aware of a large Swedish cohort study that reports on, among other things, life expectancy after BS [228]. While this study involves a very long follow-up, it does not, as far as we can tell, compare different bariatric procedures, but instead compares BS with routine care. However, in order to provide the interested reader with some information on possible long-term adverse events after BS, we have conducted a simplified search for non-randomised controlled studies with a follow-up longer than 5 years in two major databases. We have provided a summary table of studies published during the past 5 years in Appendix 4, Table A30.

Subgroups

Few if any of the included studies assessed differential effects of obesity surgery procedures on different subgroups (e.g. people with class II obesity, with BMI>50 (super-obesity), people with T2D or other co-morbidity). Data from people with different obesity class and different comorbidity profile are typically pooled, and with no subgroup analyses it is not possible to distinguish the effect of bariatric surgery on two different patient populations: i.e. patients with low BMI 30-35 with “heavy” T2D uncontrolled; patients with BMI > 40 with no or few T2D patients. This is problematic as the effect of each technique is arguably not the same on different populations. Thus, information that potentially could be of help in tailoring different procedures to different groups of patients is lacking. Others have suggested that the use of bariatric surgery registers may be of help to tailor bariatric surgery treatment [224].

Patient important outcomes – lack of studies and poor reporting

Patient-important outcomes like HRQOL were reported in less than half of the included studies, and in some of those studies the reporting was poor. No study reported on patient satisfaction with the procedure. Poor reporting of patient reported outcomes in bariatric surgery, causing problems for data syntheses and interpretation, was also reported in a systematic review on the topic [5].

Reporting of CVD risk reduction

Approximately 31% of all deaths worldwide are due to cardiovascular disease (CVD), and obesity is one of the major risk factors (WHO). The World Health Organization (WHO) emphasises the need for management of intermediate risk factors such as hypertension, dyslipidemia, and diabetes mellitus, in order to prevent CVD. Despite this, less than half of the included studies reported on blood pressure, lipids, and related medication use, while this presumably is routine patient data collected at follow-up, and should therefore be readily available to be included in studies on the effects of obesity surgery procedures. There is a need to assess the effects on all CVD risk factors in order to fully evaluate the complete benefit of bariatric surgery.

Comparative safety

We were not able to determine the comparative safety of the different obesity surgery procedures under study, as the type of AEs and the way these were reported varied widely across the included studies, and only a few studies used a standardised classification system, e.g. the Clavien-Dindo system [229]. This is a serious limitation with the studies included in this report, which hampered further analyses of most of these safety outcomes. Exceptions were well defined outcomes related to for example severe GERD requiring conversion surgery, micronutrient deficiencies and related morbidity requiring readmission and/or surgical intervention.

Limitations with the NMA

Our analyses have several limitations. Firstly, the NMAs produced rather scarce networks, especially for diabetes outcomes, typically with low to very low certainty of evidence. For the diabetes outcomes only data at 2 years follow-up could be used in the analysis, and neither weight loss nor diabetes control analyses could be conducted for 5 years follow-up due to no closed loops. Another problem in many of the analyses was that only single studies provided data for many of the included procedures and comparisons. Very few studies included follow-up periods longer than 5 years, illustrating why we know very little about the long-term effects of obesity surgery.

The discussion on heterogeneity in connection to (network) meta-analysis is still ongoing. There are no clear rules for when studies might be considered as homogenous enough to be included in NMA without violating the requirement of transitivity [12, 24, 25]. Decisions have to be made on a case-to-case basis. However, since we were not able to identify superior treatments in the analysis at hand, we can assume that intransitivity did not severely affect our overall results. Only one consistency analysis showed signs for inconsistency (weight: AGB – RYGB – SG loop, 3 years follow up). Consequently, the results of this loop should be taken with great caution. Finally, the chosen prior in Bayesian statistics can considerably affect the results. Since we decided to use uninformative priors for all our analyses so as not to bias the results, our credibility intervals in the random effects models are quite large [20]. Hence, additional research is needed to identify superior treatments.

The diabetes results depended heavily on the chosen statistical model. While the random effects models were mostly inconclusive, the fixed effect models showed the superiority of individual treatments. However, the random effects model is known to be too conservative in sparse networks. On the other hand, the fixed effect model does not take heterogeneity into account and assumes that all studies are homogenous, which is an overly optimistic assumption in our analysis [20]. Finally, even if there would be substantial differences between the treatments, it remains unclear why they are not associated with better weight outcomes.

Compared to our analyses, the scope of the recently published NMAs was smaller. To our knowledge, our NMA is the first that considered diabetes and weight outcomes over different follow-up times. Our analysis differs in some respects from earlier recently published NMA. Kang and Le [218] conducted an NMA on percentages of excess weight loss and mean BMI difference 1 year after the surgery. They included studies with patients 17 years of age or older, and a BMI ≥30kg/m^2. They came to the conclusion that RYGB and SG is superior to AGB in regard to weight loss. It is important to consider that their analysis was considerably smaller and they included only 3 treatments (AGB, RYGB and SG). Furthermore, they did not mention whether they have used a fixed effect or a random effects model. One should note that we also detected a tendency toward inferior efficacy of AGB in our analysis. However, due to the differences in regard to the selection criteria, especially the minimum follow-up, the inferiority of AGB was less profound in our analysis.

8 CONCLUSION

The results of this assessment suggest little or no differences in the effects of the different bariatric surgery procedures (AGB, SG, RYGB, D-RYGB, OAGB, BPD-DS, and BPD) on weight-related outcomes and diabetes control. However, our results are based mainly on low to very low certainty evidence, with few or even single studies providing data for many of the comparisons. No evidence was found for the effectiveness of the more recent SADI-S or SASI procedures. No study reported on patient satisfaction with the surgical procedure.

Improved HRQOL was consistently reported after bariatric surgery, but with little to no difference between procedures. We were unable to determine the relative effect of the different procedures on short- and long-term mortality, progression of obesity, and obesity-related co-morbidities. For most comparisons there were typically little to no difference in the effect on cardiovascular risk. Evidence from a couple of studies indicated beneficial effects of some of the more malabsorptive procedures (BPD-DS, BPD and D-RYGB) on cardiovascular risk reduction, but entailing a potentially greater risk of micronutrient deficiencies and metabolic complications. There was some evidence suggesting greater problems with insufficient weight loss and re-operations in AGB, as compared to RYGB, and a greater risk for problems with GERD in patients with SG, including a greater risk of severe GERD that required conversion surgery, as compared to RYGB.

More high-quality research is needed to determine the relative effect of most obesity surgery procedures, as results for many comparisons are based on data from few studies at high risk of bias. There is also a need for studies with longer follow-up in order to assess the long-term effects of obesity surgery. The fact that most studies do not use the same classification for adverse events, and varying definitions of other outcomes (e.g. weight regain, insufficient weight loss, treatment failure), makes comparisons difficult. There is a need for standardised definitions, uniform classifications of adverse events, and reporting standards in this field of research to improve the evidence base.

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APPENDIX 1: METHODS AND DESCRIPTION OF THE EVIDENCE USED

DOCUMENTATION OF THE SEARCH STRATEGIES

[Include detailed tables on searches conducted in databases, study registries and other sources. Complete search strategies should be presented for each source separately. The SOP on "Information Retrieval" in the Companion Guide shall be consulted for further guidance.]

OTCA26 Obesity surgery – Search I: Systematic Reviews and HTA

Database	Search date	Hits	Comment
Cochrane Database of Systematic Reviews (Wiley)	23.04.2020	12	2013-2020
Embase (Ovid)	23.04.2020	1602	2013-2020
Epistemonikos	23.04.2020	1004	2013-2020
MEDLINE (Ovid)	23.04.2020	1355	2013-2020
PROSPERO (NIHR)	23.04.2020	307	International prospective register of systematic reviews
Web of Science Core Collection	22.04.2020	2523	2013-2020
Total (with duplicates)		6803	Export to EndNote

Database: Cochrane Database of Systematic Reviews

ID	Search	Hits
#1	MeSH descriptor: [Bariatric Surgery] this term only	262
#2	MeSH descriptor: [Gastric Bypass] this term only	444
#3	MeSH descriptor: [Gastroplasty] this term only	176
#4	MeSH descriptor: [Biliopancreatic Diversion] this term only	26
#5	MeSH descriptor: [Anastomosis, Roux-en-Y] this term only	124
#6	MeSH descriptor: [Jejunoileal Bypass] this term only	21
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	938
#8	(((bariatric* or metabolic or "weight loss" or endobariatric* or obes* or superobes* or scopinaro or restrictive) NEAR/3 (surg* or operation* or	4825

	procedure*))):ti,ab,kw (Word variations have been searched)	
#9	(“gastric bypass”):ti,ab,kw (Word variations have been searched)	1739
#10	(Roux-en-Y):ti,ab,kw (Word variations have been searched)	1315
#11	(RYGB):ti,ab,kw (Word variations have been searched)	547
#12	(LRYGB):ti,ab,kw (Word variations have been searched)	142
#13	(“distal gastric bypass”):ti,ab,kw (Word variations have been searched)	9
#14	(“distal roux-en-y“):ti,ab,kw (Word variations have been searched)	0
#15	(“mini gastric bypass“):ti,ab,kw (Word variations have been searched)	51
#16	(LMGB):ti,ab,kw (Word variations have been searched)	8
#17	(“one anastomosis gastric bypass“):ti,ab,kw (Word variations have been searched)	59
#18	(“single anastomosis gastric bypass“):ti,ab,kw (Word variations have been searched)	7
#19	(OAGB):ti,ab,kw (Word variations have been searched)	52
#20	(OAGB-MGB):ti,ab,kw (Word variations have been searched)	13
#21	(SAGB):ti,ab,kw (Word variations have been searched)	19
#22	(“omega loop gastric bypass“):ti,ab,kw (Word variations have been searched)	16
#23	(SADI-S):ti,ab,kw (Word variations have been searched)	7
#24	(((sleeve or subtotal) NEAR/3 (gastrectom* or gastric))):ti,ab,kw (Word variations have been searched)	1159
#25	(LVSG):ti,ab,kw (Word variations have been searched)	1
#26	(LSG):ti,ab,kw (Word variations have been searched)	351
#27	(LISG):ti,ab,kw (Word variations have been searched)	1
#28	(((gastric or stomach) NEXT (banding or bypass or mini-bypass or minibypass or sleeve))):ti,ab,kw (Word variations have been searched)	1998
#29	(LAGB):ti,ab,kw (Word variations have been searched)	101
#30	(gastroplast*):ti,ab,kw (Word variations have been searched)	317
#31	(gastro-plast*):ti,ab,kw (Word variations have been searched)	0
#32	(lapband* OR lap-band*):ti,ab,kw (Word variations have been searched)	46

#33	(gastroduodenostom*):ti,ab,kw (Word variations have been searched)	25
#34	(gastroenterostom*):ti,ab,kw (Word variations have been searched)	95
#35	(hemigastrectom*):ti,ab,kw (Word variations have been searched)	2
#36	(duodenal NEXT switch*):ti,ab,kw (Word variations have been searched)	68
#37	(BDDS):ti,ab,kw (Word variations have been searched)	4
#38	(BPD-DS):ti,ab,kw (Word variations have been searched)	20
#39	(((biliary-pancreatic or biliopancreatic or pancreatobiliary or pancreatic-biliary) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))):ti,ab,kw (Word variations have been searched)	111
#40	(((duodenojejunal or duodenal-jejunal) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))):ti,ab,kw (Word variations have been searched)	47
#41	(((gastroileal or gastro-ileal or gastric-ileal) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))):ti,ab,kw (Word variations have been searched)	0
#42	(((gastrointestinal or gastro-intestinal) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))):ti,ab,kw (Word variations have been searched)	28
#43	(((gastrojejunal or gastric-jejunal) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))):ti,ab,kw (Word variations have been searched)	5
#44	(((ileojejunal or ileal-jejunal or ileal*) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))):ti,ab,kw (Word variations have been searched)	84
#45	(((jejunoileal or jejunal-ileal) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))):ti,ab,kw (Word variations have been searched)	66
#46	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45	6285
#47	#7 OR #46	6285
#48	MeSH descriptor: [Obesity, Morbid] this term only	1125
#49	MeSH descriptor: [Obesity] this term only	11005
#50	#48 OR #49	11986

#51	(obes*):ti,ab,kw (Word variations have been searched)	39675
#52	(superobes*):ti,ab,kw (Word variations have been searched)	47
#53	#51 OR #52	39677
#54	#50 OR #53	39677
#55	#47 AND #54	3454
#56	#47 AND #54 with Cochrane Library publication date Between Jan 2013 and Apr 2020, in Cochrane Reviews, Cochrane Protocols	12

Database: Embase 1974 to 2020 April 22

#	Searches	Results
1	bariatric surgery/	31184
2	gastric bypass surgery/	3641
3	gastroplasty/	4204
4	biliopancreatic bypass/	3343
5	Roux-en-Y gastric bypass/	6621
6	jejunoileal bypass/	708
7	or/1-6 [Subject Heading]	42247
8	((bariatric* or metabolic or weight loss or endobariatric* or obes* or superobes* or scopinaro or restrictive) adj3 (surg* or operation* or procedure*)).ti,ab,kw.	45548
9	gastric bypass.ti,ab,kw.	22330
10	Roux-en-Y.ti,ab,kw.	19466
11	RYGB.ti,ab,kw.	6634
12	LRYGB.ti,ab,kw.	2013
13	distal gastric bypass.ti,ab,kw.	77
14	distal roux-en-y.ti,ab,kw.	35
15	mini gastric bypass.ti,ab,kw.	680
16	LMGB.ti,ab,kw.	92
17	one anastomosis gastric bypass.ti,ab,kw.	577

18	single anastomosis gastric bypass.ti,ab,kw.	117
19	OAGB.ti,ab,kw.	476
20	OAGB-MGB.ti,ab,kw.	162
21	SAGB.ti,ab,kw.	219
22	omega loop gastric bypass.ti,ab,kw.	132
23	SADI-S.ti,ab,kw.	135
24	((sleeve or subtotal) adj3 gastrectom*).ti,ab,kw.	15847
25	LVSG.ti,ab,kw.	29
26	LSG.ti,ab,kw.	4988
27	LISG.ti,ab,kw.	4
28	((gastric or stomach) adj (banding or bypass or mini-bypass or minibypass or sleeve)).ti,ab,kw.	25951
29	LAGB.ti,ab,kw.	2366
30	gastroplast*.ti,ab,kw.	3084
31	gastro-plast*.ti,ab,kw.	10
32	(lap-band* or lapband*).ti,ab,kw.	683
33	gastroduodenostom*.ti,ab,kw.	405
34	gastroenterostom*.ti,ab,kw.	841
35	hemigastrectom*.ti,ab,kw.	108
36	duodenal switch*.ti,ab,kw.	1618
37	BDDS.ti,ab,kw.	78
38	BPD-DS.ti,ab,kw.	407
39	((biliary-pancreatic or biliopancreatic or pancreatobiliary or pancreatic-biliary) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	1927
40	((duodenojejunal or duodenal-jejunal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	579
41	((gastroileal or gastro-ileal or gastric-ileal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	12
42	((gastrointestinal or gastro-intestinal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	215

43	((gastrojejunal or gastric-jejunal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	90
44	((ileojejunal or ileal-jejunal or ileal*) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	1772
45	((jejunoileal or jejunal-ileal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	1019
46	or/8-45 [Text words]	70440
47	7 or 46 [Subject Heading OR Text words]	76377
48	morbid obesity/	21077
49	obesity/	415699
50	or/48-49	431946
51	obes*.ti,ab,kw.	449073
52	superobes*.ti,ab,kw.	395
53	or/51-52	449160
54	50 or 53	559975
55	47 and 54 [Without filter]	47178
56	(recommendation* or consensus or guidance or guideline*).ti. or (practice guideline/or consensus development/) or (Guideline or Practice Guideline).pt.	529526
57	Health Technology assessment.ti,ab,kw.	6463
58	hta.ti,ab,kw.	6606
59	systematic review.kw. or literature/	68424
60	meta-analysis.pt. or meta analysis/	184915
61	((systematic* or literature) adj3 (overview or review* or search*)).ti,ab.	580024
62	(meta-anal* or metaanal* or meta-regression* or umbrella review* or overview of reviews or review of reviews or (evidence* adj2 synth*) or synthesis review*).ti,ab.	231843
63	or/56-62 [SR filter]	1260345
64	55 and 63 [Subject AND SR filter]	3711
65	limit 64 to yr="2013 -Current"	2524
66	limit 65 to embase	1602

Database: Epistemonikos (Advanced search – Title/Abstract)
SR 947, BR 18, SS 39 – Total 1004 hits

(title:((title:(((bariatric* OR metabolic OR “weight loss“ OR endobariatric* OR obes* OR superobes* OR scopinaro OR restrictive) AND (surg* OR operation* OR procedure*)) OR “gastric bypass“ OR Roux-en-Y OR “Roux en Y“ OR RYGB OR LRYGB OR “distal gastric bypass“ OR “distal roux en y“ OR “mini gastric bypass“ OR LMGB OR “one anastomosis gastric bypass“ OR “single anastomosis gastric bypass“ OR OAGB OR OAGB-MGB OR SAGB OR “omega loop gastric bypass“ OR SADI-S OR LVSG OR LSG OR LISG OR ((sleeve OR subtotal) AND gastrectom*) OR ((gastric OR stomach) AND (banding OR bypass OR mini-bypass OR minibypass OR sleeve)) OR LAGB OR gastroplast* OR gastro-plast* OR “gastro plast“ OR lap-band* OR “lap band“ OR lapband* OR gastroduodenostom* OR hemigastrectom* OR “duodenal switch“ OR BDDS OR BPD-DS OR ((biliary-pancreatic OR “biliary pancreatic“ OR biliopancreatic OR pancreatobiliary OR pancreatic-biliary OR “pancreatic biliary“ OR duodenojejunal OR duodenal-jejunal OR “duodenal jejunal“ OR gastroileal OR gastro-ileal OR “gastro ileal“ OR gastricileal OR gastric-ileal OR “gastric ileal“ OR gastrointestinal OR gastro-intestinal OR “gastro intestinal“ OR gastrojejunal OR gastric-jejunal OR “gastric jejunal“ OR ileojejunal OR ileal-jejunal OR “ileal jejunal“ OR ileal* OR jejunoileal OR jejunal-ileal OR “jejunal ileal“) AND (bypass OR derivation* OR diversion* OR shunt* OR interposition*))) OR abstract:(((bariatric* OR metabolic OR “weight loss“ OR endobariatric* OR obes* OR superobes* OR scopinaro OR restrictive) AND (surg* OR operation* OR procedure*)) OR “gastric bypass“ OR Roux-en-Y OR “Roux en Y“ OR RYGB OR LRYGB OR “distal gastric bypass“ OR “distal roux en y“ OR “mini gastric bypass“ OR LMGB OR “one anastomosis gastric bypass“ OR “single anastomosis gastric bypass“ OR OAGB OR OAGB-MGB OR SAGB OR “omega loop gastric bypass“ OR SADI-S OR LVSG OR LSG OR LISG OR ((sleeve OR subtotal) AND gastrectom*) OR ((gastric OR stomach) AND (banding OR bypass OR mini-bypass OR minibypass OR sleeve)) OR LAGB OR gastroplast* OR gastro-plast* OR “gastro plast“ OR lap-band* OR “lap band“ OR lapband* OR gastroduodenostom* OR hemigastrectom* OR “duodenal switch“ OR BDDS OR BPD-DS OR ((biliary-pancreatic OR “biliary pancreatic“ OR biliopancreatic OR pancreatobiliary OR pancreatic-biliary OR “pancreatic biliary“ OR duodenojejunal OR duodenal-jejunal OR “duodenal jejunal“ OR gastroileal OR gastro-ileal OR “gastro ileal“ OR gastricileal OR gastric-ileal OR “gastric ileal“ OR gastrointestinal OR gastro-intestinal OR “gastro intestinal“ OR gastrojejunal OR gastric-jejunal OR “gastric jejunal“ OR ileojejunal OR ileal-jejunal OR “ileal jejunal“ OR ileal* OR jejunoileal OR jejunal-ileal OR “jejunal ileal“) AND (bypass OR derivation* OR diversion* OR shunt* OR interposition*)))) AND (title:(obes* OR superobes*) OR abstract:(obes* OR superobes*))) OR abstract:((title:(((bariatric* OR metabolic OR “weight loss“ OR endobariatric* OR obes* OR superobes* OR scopinaro OR restrictive) AND (surg* OR operation* OR procedure*)) OR “gastric bypass“ OR Roux-en-Y OR “Roux en Y“ OR RYGB OR LRYGB OR “distal gastric bypass“ OR “distal roux en y“ OR “mini gastric bypass“ OR LMGB OR “one anastomosis gastric bypass“ OR “single anastomosis gastric bypass“ OR OAGB OR OAGB-MGB OR SAGB OR “omega loop gastric bypass“ OR SADI-S OR LVSG OR LSG OR LISG OR ((sleeve OR subtotal) AND gastrectom*) OR ((gastric OR stomach) AND (banding OR bypass OR mini-bypass OR minibypass OR sleeve)) OR LAGB OR gastroplast* OR gastro-plast* OR “gastro plast“ OR lap-band* OR “lap band“ OR lapband* OR gastroduodenostom* OR hemigastrectom* OR “duodenal switch“ OR BDDS OR BPD-DS OR ((biliary-pancreatic OR “biliary pancreatic“ OR biliopancreatic OR pancreatobiliary OR pancreatic-biliary OR “pancreatic biliary“ OR duodenojejunal OR duodenal-jejunal OR “duodenal jejunal“ OR gastroileal OR gastro-ileal OR “gastro ileal“ OR gastricileal OR gastric-ileal OR “gastric ileal“ OR gastrointestinal OR gastro-intestinal OR “gastro intestinal“ OR gastrojejunal OR gastric-jejunal OR “gastric jejunal“ OR ileojejunal OR ileal-jejunal OR “ileal jejunal“ OR ileal* OR jejunoileal OR jejunal-ileal OR “jejunal ileal“) AND (bypass OR derivation* OR diversion* OR shunt* OR

interposition*))) OR abstract:(((bariatric* OR metabolic OR “weight loss“ OR endobariatric* OR obes* OR superobes* OR scopinaro OR restrictive) AND (surg* OR operation* OR procedure*)) OR “gastric bypass“ OR Roux-en-Y OR “Roux en Y“ OR RYGB OR LRYGB OR “distal gastric bypass“ OR “distal roux en y“ OR “mini gastric bypass“ OR LMGB OR “one anastomosis gastric bypass“ OR “single anastomosis gastric bypass“ OR OAGB OR OAGB-MGB OR SAGB OR “omega loop gastric bypass“ OR SADI-S OR LVSG OR LSG OR LISG OR ((sleeve OR subtotal) AND gastrectom*) OR ((gastric OR stomach) AND (banding OR bypass OR mini-bypass OR minibypass OR sleeve)) OR LAGB OR gastroplast* OR gastro-plast* OR “gastro plast“ OR lap-band* OR “lap band“ OR lapband* OR gastroduodenostom* OR hemigastrectom* OR “duodenal switch“ OR BDDS OR BPD-DS OR ((biliary-pancreatic OR “biliary pancreatic“ OR biliopancreatic OR pancreatobiliary OR pancreatic-biliary OR “pancreatic biliary“ OR duodenojejunal OR duodenal-jejunal OR “duodenal jejunal“ OR gastroileal OR gastro-ileal OR “gastro ileal“ OR gastricileal OR gastric-ileal OR “gastric ileal“ OR gastrointestinal OR gastro-intestinal OR “gastro intestinal“ OR gastrojejunal OR gastric-jejunal OR “gastric jejunal“ OR ileojejunal OR ileal-jejunal OR “ileal jejunal“ OR ileal* OR jejunoileal OR jejunal-ileal OR “jejunal ileal“) AND (bypass OR derivation* OR diversion* OR shunt* OR interposition*)))) AND (title:(obes* OR superobes*) OR abstract:(obes* OR superobes*)))) AND (title:((title:(((bariatric* OR metabolic OR “weight loss“ OR endobariatric* OR obes* OR superobes* OR scopinaro OR restrictive) AND (surg* OR operation* OR procedure*)) OR “gastric bypass“ OR Roux-en-Y OR “Roux en Y“ OR RYGB OR LRYGB OR “distal gastric bypass“ OR „distal roux en y“ OR „mini gastric bypass“ OR LMGB OR „one anastomosis gastric bypass“ OR „single anastomosis gastric bypass“ OR OAGB OR OAGB-MGB OR SAGB OR „omega loop gastric bypass“ OR SADI-S OR LVSG OR LSG OR LISG OR ((sleeve OR subtotal) AND gastrectom*) OR ((gastric OR stomach) AND (banding OR bypass OR mini-bypass OR minibypass OR sleeve)) OR LAGB OR gastroplast* OR gastro-plast* OR „gastro plast“ OR lap-band* OR „lap band“ OR lapband* OR gastroduodenostom* OR hemigastrectom* OR „duodenal switch“ OR BDDS OR BPD-DS OR ((biliary-pancreatic OR „biliary pancreatic“ OR biliopancreatic OR pancreatobiliary OR pancreatic-biliary OR „pancreatic biliary“ OR duodenojejunal OR duodenal-jejunal OR „duodenal jejunal“ OR gastroileal OR gastro-ileal OR „gastro ileal“ OR gastricileal OR gastric-ileal OR „gastric ileal“ OR gastrointestinal OR gastro-intestinal OR „gastro intestinal“ OR gastrojejunal OR gastric-jejunal OR „gastric jejunal“ OR ileojejunal OR ileal-jejunal OR „ileal jejunal“ OR ileal* OR jejunoileal OR jejunal-ileal OR „jejunal ileal“) AND (bypass OR derivation* OR diversion* OR shunt* OR interposition*))) OR abstract:(((bariatric* OR metabolic OR „weight loss“ OR endobariatric* OR obes* OR superobes* OR scopinaro OR restrictive) AND (surg* OR operation* OR procedure*)) OR „gastric bypass“ OR Roux-en-Y OR „Roux en Y“ OR RYGB OR LRYGB OR „distal gastric bypass“ OR „distal roux en y“ OR „mini gastric bypass“ OR LMGB OR „one anastomosis gastric bypass“ OR „single anastomosis gastric bypass“ OR OAGB OR OAGB-MGB OR SAGB OR „omega loop gastric bypass“ OR SADI-S OR LVSG OR LSG OR LISG OR ((sleeve OR subtotal) AND gastrectom*) OR ((gastric OR stomach) AND (banding OR bypass OR mini-bypass OR minibypass OR sleeve)) OR LAGB OR gastroplast* OR gastro-plast* OR „gastro plast“ OR lap-band* OR „lap band“ OR lapband* OR gastroduodenostom* OR hemigastrectom* OR „duodenal switch“ OR BDDS OR BPD-DS OR ((biliary-pancreatic OR „biliary pancreatic“ OR biliopancreatic OR pancreatobiliary OR pancreatic-biliary OR „pancreatic biliary“ OR duodenojejunal OR duodenal-jejunal OR „duodenal jejunal“ OR gastroileal OR gastro-ileal OR „gastro ileal“ OR gastricileal OR gastric-ileal OR „gastric ileal“ OR gastrointestinal OR gastro-intestinal OR „gastro intestinal“ OR gastrojejunal OR gastric-jejunal OR „gastric jejunal“ OR ileojejunal OR ileal-jejunal OR „ileal jejunal“ OR ileal* OR jejunoileal OR jejunal-ileal OR „jejunal ileal“) AND (bypass OR derivation* OR diversion* OR shunt* OR interposition*)))) AND (title:(obes* OR superobes*) OR abstract:(obes* OR superobes*))) OR abstract:((title:(((bariatric* OR metabolic OR „weight loss“ OR endobariatric* OR obes* OR superobes* OR scopinaro OR restrictive) AND (surg* OR

operation* OR procedure*)) OR „gastric bypass“ OR Roux-en-Y OR „Roux en Y“ OR RYGB OR LRYGB OR „distal gastric bypass“ OR „distal roux en y“ OR „mini gastric bypass“ OR LMGB OR „one anastomosis gastric bypass“ OR „single anastomosis gastric bypass“ OR OAGB OR OAGB-MGB OR SAGB OR „omega loop gastric bypass“ OR SADI-S OR LVSG OR LSG OR LISG OR ((sleeve OR subtotal) AND gastrectom*) OR ((gastric OR stomach) AND (banding OR bypass OR mini-bypass OR minibypass OR sleeve)) OR LAGB OR gastroplast* OR gastro-plast* OR „gastro plast“ OR lap-band* OR „lap band“ OR lapband* OR gastroduodenostom* OR hemigastrectom* OR „duodenal switch“ OR BDDS OR BPD-DS OR ((biliary-pancreatic OR „biliary pancreatic“ OR biliopancreatic OR pancreatobiliary OR pancreatic-biliary OR „pancreatic biliary“ OR duodenojejunal OR duodenal-jejunal OR „duodenal jejunal“ OR gastroileal OR gastro-ileal OR „gastro ileal“ OR gastricileal OR gastric-ileal OR „gastric ileal“ OR gastrointestinal OR gastro-intestinal OR „gastro intestinal“ OR gastrojejunal OR gastric-jejunal OR „gastric jejunal“ OR ileojejunal OR ileal-jejunal OR „ileal jejunal“ OR ileal* OR jejunoileal OR jejunal-ileal OR „jejunal ileal“) AND (bypass OR derivation* OR diversion* OR shunt* OR interposition*))) OR abstract:(((bariatric* OR metabolic OR „weight loss“ OR endobariatric* OR obes* OR superobes* OR scopinaro OR restrictive) AND (surg* OR operation* OR procedure*)) OR „gastric bypass“ OR Roux-en-Y OR „Roux en Y“ OR RYGB OR LRYGB OR „distal gastric bypass“ OR „distal roux en y“ OR „mini gastric bypass“ OR LMGB OR „one anastomosis gastric bypass“ OR „single anastomosis gastric bypass“ OR OAGB OR OAGB-MGB OR SAGB OR „omega loop gastric bypass“ OR SADI-S OR LVSG OR LSG OR LISG OR ((sleeve OR subtotal) AND gastrectom*) OR ((gastric OR stomach) AND (banding OR bypass OR mini-bypass OR minibypass OR sleeve)) OR LAGB OR gastroplast* OR gastro-plast* OR „gastro plast“ OR lap-band* OR „lap band“ OR lapband* OR gastroduodenostom* OR hemigastrectom* OR „duodenal switch“ OR BDDS OR BPD-DS OR ((biliary-pancreatic OR „biliary pancreatic“ OR biliopancreatic OR pancreatobiliary OR pancreatic-biliary OR „pancreatic biliary“ OR duodenojejunal OR duodenal-jejunal OR „duodenal jejunal“ OR gastroileal OR gastro-ileal OR „gastro ileal“ OR gastricileal OR gastric-ileal OR „gastric ileal“ OR gastrointestinal OR gastro-intestinal OR „gastro intestinal“ OR gastrojejunal OR gastric-jejunal OR „gastric jejunal“ OR ileojejunal OR ileal-jejunal OR „ileal jejunal“ OR ileal* OR jejunoileal OR jejunal-ileal OR „jejunal ileal“) AND (bypass OR derivation* OR diversion* OR shunt* OR interposition*)))) AND (title:(obes* OR superobes*) OR abstract:(obes* OR superobes*))))

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to April 22, 2020

#	Searches	Results
1	Bariatric Surgery/	9782
2	Gastric Bypass/	9155
3	Gastroplasty/	4263
4	Biliopancreatic Diversion/	988
5	Anastomosis, Roux-en-Y/	3468
6	Jejunoileal Bypass/	597
7	or/1-6 [Subject Heading]	24668

8	((bariatric* or metabolic or weight loss or endobariatric* or obes* or superobes* or scopinaro or restrictive) adj3 (surg* or operation* or procedure*)).ti,ab,kf.	25222
9	gastric bypass.ti,ab,kf.	11442
10	Roux-en-Y.ti,ab,kf.	11068
11	RYGB.ti,ab,kf.	2946
12	LRYGB.ti,ab,kf.	845
13	distal gastric bypass.ti,ab,kf.	47
14	distal roux-en-y.ti,ab,kf.	31
15	mini gastric bypass.ti,ab,kf.	263
16	LMGB.ti,ab,kf.	34
17	one anastomosis gastric bypass.ti,ab,kf.	252
18	single anastomosis gastric bypass.ti,ab,kf.	52
19	OAGB.ti,ab,kf.	174
20	OAGB-MGB.ti,ab,kf.	32
21	SAGB.ti,ab,kf.	123
22	omega loop gastric bypass.ti,ab,kf.	51
23	SADI-S.ti,ab,kf.	38
24	((sleeve or subtotal) adj3 gastrectom*).ti,ab,kf.	7602
25	LVSG.ti,ab,kf.	11
26	LSG.ti,ab,kf.	2037
27	LISG.ti,ab,kf.	5
28	((gastric or stomach) adj (banding or bypass or mini-bypass or minibypass or sleeve)).ti,ab,kf.	13466
29	LAGB.ti,ab,kf.	1149
30	gastroplast*.ti,ab,kf.	2044
31	gastro-plast*.ti,ab,kf.	2
32	lap-band*or lapband*.ti,ab,kf.	0
33	gastroduodenostom*.ti,ab,kf.	372

34	gastroenterostom*.ti,ab,kf.	1313
35	hemigastrectom*.ti,ab,kf.	118
36	duodenal switch*.ti,ab,kf.	759
37	BDDS.ti,ab,kf.	53
38	BPD-DS.ti,ab,kf.	169
39	((biliary-pancreatic or biliopancreatic or pancreatobiliary or pancreatic-biliary) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	1188
40	((duodenojejunal or duodenal-jejunal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	297
41	((gastroileal or gastro-ileal or gastric-ileal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	6
42	((gastrointestinal or gastro-intestinal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	128
43	((gastrojejunal or gastric-jejunal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	54
44	((ileojejunal or ileal-jejunal or ileal*) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	1182
45	((jejunoileal or jejunal-ileal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	882
46	or/8-45 [Text words]	42529
47	7 or 46 [Subject Heading OR Text words]	46239
48	Obesity, Morbid/	19241
49	Obesity/	177855
50	or/48-49	195858
51	obes*.ti,ab,kf.	301072
52	superobes*.ti,ab,kf.	203
53	or/51-52	301120
54	50 or 53	344303
55	47 and 54 [Without filter]	28074
56	(recommendation* or consensus or guidance or guideline*).ti. or (Guideline/or Practice Guideline/or Consensus Development	165529

	Conference/) or (Guideline or Practice Guideline).pt.	
57	Health Technology assessment.ti,ab,kw.	4665
58	hta.ti,ab,kf.	3024
59	systematic review.kw. or Review Literature as Topic/	23957
60	meta-analysis.pt. or Meta-Analysis as Topic/	130350
61	((systematic* or literature) adj3 (overview or review* or search*)).ti,ab.	477971
62	(meta-anal* or metaanal* or meta-regression* or umbrella review* or overview of reviews or review of reviews or (evidence* adj2 synth*) or synthesis review*).ti,ab.	178019
63	or/56-62 [SR filter]	743715
64	55 and 63 [Subject AND SR filter]	1983
65	limit 64 to yr="2013 -Current"	1355

Database: PROSPERO – International prospective register of systematic reviews

#	Search	Results
#1	MeSH DESCRIPTOR Bariatric Surgery EXPLODE ALL TREES	225
#2	MeSH DESCRIPTOR Gastric Bypass EXPLODE ALL TREES	36
#3	"bariatric surgery" OR "gastric bypass"	380
#4	#1 OR #2 OR #3	392
#5	MeSH DESCRIPTOR Obesity, Morbid EXPLODE ALL TREES	75
#6	MeSH DESCRIPTOR Obesity EXPLODE ALL TREES	1186
#7	obes* OR superobes*	3514
#8	#5 OR #6 OR #7	3568
#9	#4 AND #8	307

Database: Web of Science Core Collection

Set	Search	Results

# 1	TOPIC: (((bariatric* OR “metabolic“ OR “weight loss“ OR endobariatric* OR obes* OR superobes* OR “scopinaro“ OR “restrictive“) NEAR/2 (surg* OR operation* OR procedure*))) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	21,813
# 2	TOPIC: (“gastric bypass“ OR “Roux-en-Y“ OR “Roux en Y“ OR “RYGB“ OR “LRYGB“ OR “distal gastric bypass“ OR “distal roux-en-y“ OR “distal roux en y“ OR „mini gastric bypass“ OR „LMGB“ OR „one anastomosis gastric bypass“ OR „single anastomosis gastric bypass“ OR „OAGB“ OR „OAGB-MGB“ OR „SAGB“ OR „omega loop gastric bypass“ OR „SADI-S“ OR „LVSG“ OR „LSG“ OR „LISG“) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	15,471
# 3	TOPIC: (((„sleeve“ OR „subtotal“) NEAR/2 gastrectom*)) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	8,921
# 4	TOPIC: ((((„gastric“ OR „stomach“) NEAR/0 („banding“ OR „bypass“ OR „mini-bypass“ OR „minibypass“ OR „sleeve“))) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	13,875
# 5	TOPIC: („LAGB“ OR gastroplast* OR gastro-plast* OR „gastro plast“ OR lap-band* OR „lap band“ OR lapband* OR gastroduodenostom* OR hemigastrectom* OR „duodenal switch“ OR „BDDS“ OR „BPD-DS“) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	2,339
# 6	TOPIC: ((((„biliary-pancreatic“ OR „biliopancreatic“ OR „pancreatobiliary“ OR „pancreatic-biliary“ OR „pancreatic biliary“ OR „duodenojejunal“ OR „duodenal-jejunal“ OR „duodenal jejunal“ OR „gastroileal“ OR „gastro-ileal“ OR „gastro ileal“ OR „gastricileal“ OR „gastric-ileal“ OR „gastric ileal“ OR „gastrointestinal“ OR „gastro-intestinal“ OR „gastro intestinal“ OR „gastrojejunal“ OR „gastric-jejunal“ OR „gastric jejunal“ OR „ileojejunal“ OR „ileal-jejunal“ OR „ileal jejunal“ OR ileal* OR „jejunoileal“ OR „jejunal-ileal“ OR „jejunal ileal“) NEAR/1 („bypass“ OR derivation* or diversion* or shunt* or interposition*))) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	1,640
# 7	#6 OR #5 OR #4 OR #3 OR #2 OR #1 Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	32,491
# 8	TOPIC: (obes* OR superobes*) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	208,157
# 9	#8 AND #7 Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	16,346
# 10	TOPIC: (recommendation* OR „consensus“ OR „guidance“ OR guideline* OR „health technology assessment“ OR „hta“ OR „systematic review“ OR „meta-	775,711

	analysis“ OR „meta analysis“) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	
# 11	TOPIC: (((systematic* OR literature*) NEAR/2 (overview* or review* or search*))) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	304,267
# 12	#11 OR #10 Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	911,741
# 13	#12 AND #9 Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	2,523

OTCA26 Obesity surgery – Search II: Primary Studies

Database	Search date	Hits	Comment
Cochrane Central Register of Controlled Trials, Issue 5 of 12, May 2020	26.05.2020	3180	2013-2020
Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to May 22, 2020	26.05.2020	499	2020
Embase 1974 to 2020 May 22	26.05.2020	245	2020
Web of Science Core Collection	26.05.2020	2238	2013-2020
Total (with duplicates)		6162	Export to EndNote

Database: Cochrane Central Register of Controlled Trials, Issue 5 of 12, May 2020

ID	Search	Hits
#1	MeSH descriptor: [Bariatric Surgery] this term only	267
#2	MeSH descriptor: [Gastric Bypass] this term only	448
#3	MeSH descriptor: [Gastroplasty] this term only	176
#4	MeSH descriptor: [Biliopancreatic Diversion] this term only	26
#5	MeSH descriptor: [Anastomosis, Roux-en-Y] this term only	124
#6	MeSH descriptor: [Jejunoileal Bypass] this term only	21

#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	947
#8	(((bariatric* or metabolic or “weight loss” or endobariatric* or obes* or superobes* or scopinaro or restrictive) NEAR/3 (surg* or operation* or procedure*))) (Word variations have been searched)	6536
#9	(“gastric bypass”) (Word variations have been searched)	1804
#10	(Roux-en-Y) (Word variations have been searched)	1366
#11	(RYGB) (Word variations have been searched)	555
#12	(LRYGB) (Word variations have been searched)	144
#13	(“distal gastric bypass”) (Word variations have been searched)	9
#14	(“distal roux-en-y“) (Word variations have been searched)	0
#15	(“mini gastric bypass“) (Word variations have been searched)	51
#16	(LMGB) (Word variations have been searched)	8
#17	(“one anastomosis gastric bypass“) (Word variations have been searched)	60
#18	(“single anastomosis gastric bypass“) (Word variations have been searched)	7
#19	(OAGB) (Word variations have been searched)	53
#20	(OAGB-MGB) (Word variations have been searched)	13
#21	(SAGB) (Word variations have been searched)	19
#22	(“omega loop gastric bypass“) (Word variations have been searched)	16
#23	(SADI-S) (Word variations have been searched)	11
#24	(((sleeve or subtotal) NEAR/3 (gastrectom* or gastric))) (Word variations have been searched)	1199
#25	(LVSG) (Word variations have been searched)	1
#26	(LSG) (Word variations have been searched)	371
#27	(LISG) (Word variations have been searched)	1
#28	(((gastric or stomach) NEXT (banding or bypass or mini-bypass or minibypass or sleeve))) (Word variations have been searched)	2073
#29	(LAGB) (Word variations have been searched)	106
#30	(gastroplast*) (Word variations have been searched)	335
#31	(gastro-plast*) (Word variations have been searched)	0

#32	(lapband* OR lap-band*) (Word variations have been searched)	56
#33	(gastroduodenostom*) (Word variations have been searched)	26
#34	(gastroenterostom*) (Word variations have been searched)	106
#35	(hemigastrectom*) (Word variations have been searched)	2
#36	(duodenal NEXT switch*) (Word variations have been searched)	76
#37	(BDDS) (Word variations have been searched)	4
#38	(BPD-DS) (Word variations have been searched)	21
#39	(((biliary-pancreatic or biliopancreatic or pancreatobiliary or pancreatic-biliary) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))) (Word variations have been searched)	121
#40	(((duodenojejunal or duodenal-jejunal) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))) (Word variations have been searched)	47
#41	(((gastroileal or gastro-ileal or gastric-ileal) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))) (Word variations have been searched)	2
#42	(((gastrointestinal or gastro-intestinal) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))) (Word variations have been searched)	51
#43	(((gastrojejunal or gastric-jejunal) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))) (Word variations have been searched)	7
#44	(((ileojejunal or ileal-jejunal or ileal*) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))) (Word variations have been searched)	98
#45	(((jejunoileal or jejunal-ileal) NEAR/2 (bypass or derivation* or diversion* or shunt* or interposition*))) (Word variations have been searched)	75
#46	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45	5609
#47	#7 OR #46	5609
#48	MeSH descriptor: [Obesity, Morbid] this term only	1138
#49	MeSH descriptor: [Obesity] this term only	11060

#50	#48 OR #49	12052
#51	(obes*) (Word variations have been searched)	43103
#52	(superobes*) (Word variations have been searched)	50
#53	#51 OR #52	43105
#54	#50 OR #53	43105
#55	#47 AND #54	3870
#56	#47 AND #54 in Trials	3773
#57	#56 with Cochrane Library publication date Between Jan 2013 and May 2020	3180
#58	#56 with Publication Year from 2013 to 2020, in Trials	2642
#59	#57 OR #58	3180

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to May 22, 2020

#	Searches	Results
1	Bariatric Surgery/	9971
2	Gastric Bypass/	9277
3	Gastroplasty/	4277
4	Biliopancreatic Diversion/	992
5	Anastomosis, Roux-en-Y/	3482
6	Jejunoileal Bypass/	597
7	or/1-6 [Subject Heading]	24975
8	((bariatric* or metabolic or weight loss or endobariatric* or obes* or superobes* or scopinaro or restrictive) adj3 (surg* or operation* or procedure*)).ti,ab,kf.	25518
9	gastric bypass.ti,ab,kf.	11575
10	Roux-en-Y.ti,ab,kf.	11196
11	RYGB.ti,ab,kf.	3002
12	LRYGB.ti,ab,kf.	851
13	distal gastric bypass.ti,ab,kf.	47

14	distal roux-en-y.ti,ab,kf.	32
15	mini gastric bypass.ti,ab,kf.	266
16	LMGB.ti,ab,kf.	34
17	one anastomosis gastric bypass.ti,ab,kf.	267
18	single anastomosis gastric bypass.ti,ab,kf.	52
19	OAGB.ti,ab,kf.	185
20	OAGB-MGB.ti,ab,kf.	37
21	SAGB.ti,ab,kf.	123
22	omega loop gastric bypass.ti,ab,kf.	51
23	SADI-S.ti,ab,kf.	38
24	((sleeve or subtotal) adj3 gastrectom*).ti,ab,kf.	7717
25	LVSG.ti,ab,kf.	11
26	LSG.ti,ab,kf.	2060
27	LISG.ti,ab,kf.	5
28	((gastric or stomach) adj (banding or bypass or mini-bypass or minibypass or sleeve)).ti,ab,kf.	13606
29	LAGB.ti,ab,kf.	1151
30	gastroplast*.ti,ab,kf.	2055
31	gastro-plast*.ti,ab,kf.	2
32	lap-band*or lapband*.ti,ab,kf.	0
33	gastroduodenostom*.ti,ab,kf.	374
34	gastroenterostom*.ti,ab,kf.	1317
35	hemigastrectom*.ti,ab,kf.	118
36	duodenal switch*.ti,ab,kf.	769
37	BDDS.ti,ab,kf.	54
38	BPD-DS.ti,ab,kf.	172
39	((biliary-pancreatic or biliopancreatic or pancreatobiliary or pancreatic-biliary) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	1197
40	((duodenojejunal or duodenal-jejunal) adj2 (bypass or derivation* or	299

	diversion* or shunt* or interposition*)).ti,ab,kf.	
41	((gastroileal or gastro-ileal or gastric-ileal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	6
42	((gastrointestinal or gastro-intestinal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	129
43	((gastrojejunal or gastric-jejunal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	55
44	((ileojejunal or ileal-jejunal or ileal*) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	1187
45	((jejunoileal or jejunal-ileal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kf.	883
46	or/8-45 [Text words]	42928
47	7 or 46 [Subject Heading OR Text words]	46659
48	Obesity, Morbid/	19449
49	Obesity/	178737
50	or/48-49	196933
51	obes*.ti,ab,kf.	303308
52	superobes*.ti,ab,kf.	203
53	or/51-52	303356
54	50 or 53	346702
55	47 and 54 [Without filters]	28362
56	(“randomized controlled trial“ or “controlled clinical trial“).pt. or (randomized or randomised or randomly or rct or trial).tw,kf,bt.	1357545
57	(impact or effect).ti. or (controlled or control group*).ti,ab.	2183850
58	Randomized Controlled Trial/	506131
59	Random Allocation/	102805
60	Randomized Controlled Trials as Topic/	133039
61	or/56-60 [RCT filter]	3105768
62	55 and 61	5035
63	2020*.dt,dp,ed,ep,yr.	1026018
64	62 and 63	499

Database: Embase 1974 to 2020 May 22

#	Searches	Results
1	bariatric surgery/	31368
2	gastric bypass surgery/	3686
3	gastroplasty/	4220
4	biliopancreatic bypass/	3366
5	Roux-en-Y gastric bypass/	6741
6	jejunoileal bypass/	711
7	or/1-6 [Subject Heading]	42547
8	((bariatric* or metabolic or weight loss or endobariatric* or obes* or superobes* or scopinaro or restrictive) adj3 (surg* or operation* or procedure*)).ti,ab,kw.	45876
9	gastric bypass.ti,ab,kw.	22460
10	Roux-en-Y.ti,ab,kw.	19592
11	RYGB.ti,ab,kw.	6678
12	LRYGB.ti,ab,kw.	2024
13	distal gastric bypass.ti,ab,kw.	77
14	distal roux-en-y.ti,ab,kw.	36
15	mini gastric bypass.ti,ab,kw.	684
16	LMGB.ti,ab,kw.	92
17	one anastomosis gastric bypass.ti,ab,kw.	595
18	single anastomosis gastric bypass.ti,ab,kw.	118
19	OAGB.ti,ab,kw.	486
20	OAGB-MGB.ti,ab,kw.	165
21	SAGB.ti,ab,kw.	223
22	omega loop gastric bypass.ti,ab,kw.	132
23	SADI-S.ti,ab,kw.	136
24	((sleeve or subtotal) adj3 gastrectom*).ti,ab,kw.	15976

25	LVSG.ti,ab,kw.	29
26	LSG.ti,ab,kw.	5016
27	LISG.ti,ab,kw.	4
28	((gastric or stomach) adj (banding or bypass or mini-bypass or minibypass or sleeve)).ti,ab,kw.	26091
29	LAGB.ti,ab,kw.	2371
30	gastroplast*.ti,ab,kw.	3103
31	gastro-plast*.ti,ab,kw.	10
32	(lap-band* or lapband*).ti,ab,kw.	684
33	gastroduodenostom*.ti,ab,kw.	408
34	gastroenterostom*.ti,ab,kw.	844
35	hemigastrectom*.ti,ab,kw.	108
36	duodenal switch*.ti,ab,kw.	1628
37	BDDS.ti,ab,kw.	79
38	BPD-DS.ti,ab,kw.	410
39	((biliary-pancreatic or biliopancreatic or pancreatobiliary or pancreatic-biliary) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	1936
40	((duodenojejunal or duodenal-jejunal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	584
41	((gastroileal or gastro-ileal or gastric-ileal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	12
42	((gastrointestinal or gastro-intestinal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	216
43	((gastrojejunal or gastric-jejunal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	91
44	((ileojejunal or ileal-jejunal or ileal*) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	1780
45	((jejunoileal or jejunal-ileal) adj2 (bypass or derivation* or diversion* or shunt* or interposition*)).ti,ab,kw.	1021
46	or/8-45 [Text words]	70909
47	7 or 46 [Subject Heading OR Text words]	76878

48	morbid obesity/	21165
49	obesity/	417545
50	or/48-49	433866
51	obes*.ti,ab,kw.	451626
52	superobes*.ti,ab,kw.	396
53	or/51-52	451713
54	50 or 53	562920
55	47 and 54 [Without filter]	47455
56	(randomized or randomised or randomly or rct or trial).tw,kw.	1666591
57	(impact or effect).ti. or (controlled or control group*).ti,ab.	2696983
58	randomized controlled trial/	603101
59	randomization/	86720
60	“randomized controlled trial (topic)“/	179269
61	or/56-60 [RCT filter]	3880067
62	55 and 61	8649
63	2020*.dd,yr.	814672
64	62 and 63	322
65	limit 64 to embase	245

Database: Web of Science Core Collection

#	Search	Results
# 1	TOPIC: (((bariatric* OR „metabolic“ OR „weight loss“ OR endobariatric* OR obes* OR superobes* OR „scopinaro“ OR „restrictive“) NEAR/2 (surg* OR operation* OR procedure*))) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	34,416
# 2	TOPIC: ((„gastric bypass“ OR „Roux-en-Y“ OR „Roux en Y“ OR „RYGB“ OR „LRYGB“ OR „distal gastric bypass“ OR „distal roux-en-y“ OR „distal roux en y“ OR „mini gastric bypass“ OR „LMGB“ OR „one anastomosis gastric bypass“ OR „single anastomosis gastric bypass“ OR „OAGB“ OR „OAGB-MGB“ OR „SAGB“ OR „omega loop gastric bypass“ OR „SADI-S“ OR „LVSG“ OR „LSG“ OR „LISG“))	26,332

	Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	
# 3	TOPIC: (((„sleeve“ OR „subtotal“) NEAR/2 gastrectom*)) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	11,543
# 4	TOPIC: (((„gastric“ OR „stomach“) NEAR/0 („banding“ OR „bypass“ OR „mini-bypass“ OR „minibypass“ OR „sleeve“))) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	24,447
# 5	TOPIC: ((„LAGB“ OR gastroplast* OR gastro-plast* OR „gastro plast“ OR lap-band* OR „lap band“ OR lapband* OR gastroduodenostom* OR hemigastrectom* OR „duodenal switch“ OR „BDDS“ OR „BPD-DS“)) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	6,738
# 6	TOPIC: (((„biliary-pancreatic“ OR „biliopancreatic“ OR „pancreatobiliary“ OR „pancreatic-biliary“ OR „pancreatic biliary“ OR „duodenojejunal“ OR „duodenal-jejunal“ OR „duodenal jejunal“ OR „gastroileal“ OR „gastro-ileal“ OR „gastro ileal“ OR „gastricileal“ OR „gastric-ileal“ OR „gastric ileal“ OR „gastrointestinal“ OR „gastro-intestinal“ OR „gastro intestinal“ OR „gastrojejunal“ OR „gastric-jejunal“ OR „gastric jejunal“ OR „ileojejunal“ OR „ileal-jejunal“ OR „ileal jejunal“ OR ileal* OR „jejunoileal“ OR „jejunal-ileal“ OR „jejunal ileal“) NEAR/1 („bypass“ OR derivation* OR diversion* OR shunt* OR interposition*))) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	4,019
# 7	#6 OR #5 OR #4 OR #3 OR #2 OR #1 Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	55,918
# 8	TOPIC: ((obes* OR superobes*)) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	394,302
# 9	#8 AND #7 Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	28,524
# 10	TOPIC: ((„randomized“ or „randomised“ or „randomly“ or „rct“ or „trial“)) Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	1,671,602
# 11	#10 AND #9 Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=All years	3,463
# 12	#10 AND #9 Indexes=SCI-EXPANDED, SSCI, ESCI Timespan=2013-2020	2,238

DESCRIPTION OF THE EVIDENCE USED

Table A1: Study pool of the rapid rea

Study	Available documents[a]	Study registry entries
Angrisani 2007 [28]	Angrisani 2007; Angrisani 2013	None
Arceo-Olaiz 2008 [30]	Arceo-Olaiz 2008, Zarate 2013	NCT01504685
Aasheim 2009 [32]	Aasheim 2009; Olsen 2012; Søvik 2010, 2011, 2013, Risstad 2015	NCT00327912
CONTROL [73]	Wallenius 2018, 2020	NCT01984762
DIBASY [54]	Mingrone 2012, and 2015	NCT00888836
Fahmy 2018 [40]	Fahmy 2018	None
Hedberg 2012 [42]	Hedberg 2012	None
Himpens 2006 [46]	Himpens 2006	None
Ignat 2017 [48]	Ignat 2017, Vix 2013, 2014	NCT02475590
Karamanakos 2008 [50]	Karamanakos 2008, 2011, Kehagias 2011	None
Keidar 2013 [52]	Keidar 2012, 2013	NCT00667706
Mingrone 2012 [53]	Mingrone 2012, Mingrone 2015 Capristo 2018	NCT01581801
MISO [41]	Fink 2020	DRKS00007729
Murphy 2016 [55]	Murphy 2016, 2018	NCT01486680 ACTRN12611000751976
Nguyen 2009 [56]	Nguyen 2009, 2013, 2018	NCT00247377
OSEBERG [47]	Hofsø 2019, Borgeraas 2019, Lorentzen 2020	NCT01778738
Paluszkiewicz 2012 [58]	Paluszkiewicz 2012	NCT01806506
Rasera 2016 [62]	Rasera 2016	None
Seetharamaiah 2017 [67]	Seetharamaiah 2017, Shivakumar 2018	None
Sleeve Bypass [19, 230]	Biter 2015, 2020	NTR-4741
SLEEVEPASS [45]	Salminen 2018, Grönroos 2020, Helmiö 2012, 2014, Savolainen 2019, Honka 2014, Immonen 2013, Tuulari	NCT00793143

	2017	
SMBOSS [59]	Peterli 2015, 2017, 2018, Schneider 2016	NCT00356213
STAMPEDE [64]	Schauer 2012, 2013, 2014; 2017	NCT00432809
Svanevik 2015 [35]	Risstad 2016, Svanevik 2015, 2018 and 2019	NCT00821197
Tognoni 2016 [71]	Tognoni 2016, Gentileschi 2020	NCT04228185
TRIABETES [37]	Courcoulas 2014; 2015; 2020	NCT01047735
YOMEGA [63]	Robert 2019, 2020	NCT02139813
Zhang 2014 [74]	Zhang 2014	None
a: publications, reports, clinical study reports etc.		

Table A2: List of excluded studies (full text level) with reasons for exclusion

Reference	Main reason for exclusion (full text level)
Alarcon 2019 [231]	Poster abstract
Arterburn 2016 [232]	Clinical review
Bedi 2017 [233]	Poster abstract
Berends 2019 [234]	Poster abstract
Bhandarwar 2017 [235]	Poster abstract
Casajoana 2019 [236]	Poster abstract
Elkeleny 2017 [237]	Poster abstract
Elkeleny 2017 [238]	Poster abstract
Elkeleny 2018 [239]	Poster abstract
Elzouki 2020 [240]	Review protocol
Fink 2019 [241]	Oral abstract
Finno 2019 [242]	Oral abstract
Gadiot 2017 [243]	Poster abstract
Garcia-Oria 2019	Poster abstract
Garcia-Ruiz de Gordejuela 2017 [244]	Oral abstract
Gentileschi 2019 [72]	Oral abstract
Gomez-Almendros 2019 [245]	Oral abstract
Kalarchian 2014 [246]	Self-report of side effects.
Lee 2011 [247]	BMI at BL not in line with inclusion criteria
Lee 2014 [248]	BMI at BL not in line with inclusion criteria
Lorentzon 2019 [249]	Poster abstract
Luo 2020 [250]	Poster abstract
Maghrabi 2013 [251]	Poster abstract
Malin 2013 [252]	Poster abstract
Medina 2019 [253]	Poster abstract
Medina Manuel 2019 [254]	Poster abstract
Moustafa 2016 [40]	Poster abstract

Murphy 2019 [255]	Poster abstract
Omar 2019 [256]	Treatment of metabolic syndrome.
Ospanov 2019 [257]	Unclear comparison
Ospanov 2019 [258]	Other comparison
Pucci 2015 [259]	Retrospective cross-sectional study.
Robert 2018 [260]	Conference abstract
Ruiz 2017 [261]	Poster abstract
Ruiz-Tovar 2019 [262]	Trial retracted
Ruiz-Tovar 2018 [263]	Oral abstract
Ruiz-Tovar 2018 [264]	Conference abstract
Singh 2019 [265]	Oral abstract
Spuntarelli 2015 [266]	Oral abstract
Tan 2019 [267]	Oral abstract
Tang 2016 [268]	BMI at BL not in line with inclusion criteria
Techagumpuch 2017 [269]	Oral presentation
Troung 2018 [270]	Conference abstract
Yang 2015 [271]	BMI at BL not in line with inclusion criteria
Yashkov 2018 [272]	Conference abstract

Guidelines for diagnosis and management

Table A3: Recommendations for primary bariatric surgery in adults according to public health bodies and professional societies

Country or region	Advising body	AGB	SG	RYGB	OAGB	BPD-DS	SADI-S	SASI	Other
+	Available (not in widespread use)								
++	In current use								
+++	In current use (most common procedure)								
O	Not in use								
Ø	In use for research purposes or under consideration								
-	Not recommended or endorsed								
European guidance									
Belgium	KCE 2019[83]		++	++	O	+			O*
Denmark	DHA 2017[145]		++	+++†					
England	NICE 2012,[155] 2014,[127] 2016.[97] NHS 2016[125]	++	++	++		++	Ø		Ø*
France	HAS 2020,[96] 2019,[154] 2009[150]	+	++ +	++	++‡		Ø		Ø§
Germany	DGAV 2018[142]	++	++	++	++	++			
Norway	NIPH 2014,[273]	+	++	+++	+	+¶			

	2014,[273] 2018[143]								
Spain	SECO 2015[274] and 2016[149]	++	++	++		++			
Sweden	No guidance identified[104]	+	++	+++	+				
Switzerland	SMOB 2018,[147] ASEMO 2016[146]	+	++	+++	Ø	+[#]			Ø **
The Netherlands	NHG 2010[151]	++	O	++		++			
Europe	EASO 2020[4]	- [††]	++	++	++[‡‡]	++	O		
Non-European or international guidance									
United States	AACE/TOS/ASMBS/OMA/ ASA 2019 update[117]	++	++	++	-	++[§§]			
	AACE/ACE 2016[206]		++	++		++			
Canada	Obesity Canada 2020[153]	-	++	++	-	++			
International guidance	IFSO position statement 2018[95]						++[¶]		
	Joint Statement by International Diabetes Associations 2016[85]	++	++	++		++			

Key:

*Gastric plication (KCE; NICE), variants of the RYGB or new less-established (endoscopic) techniques such as the gastric balloons, the 'endobarrier', and the transoral endoscopic gastroplication (KCE).

† RYGB is the recommended preference procedure, however use of SG is increasing.
‡ OAGB with a 200 cm (or longer) BP limb is not recommended. OAGB with a 150 cm BP limb is under consideration pending further evidence from comparative studies.
§ SADI-S, sleeve gastrectomy with transit bipartition (SG-TB) and the endosleeve are in the process of distribution in France and will be evaluated at the end of ongoing clinical studies.

¶ BPD-DS not recommended BMI <35 kg/m^2.
**Interventions in evaluation include gastric plication, implantable gastric stimulation, vagus blockade, ileal transposition, OAGB, duodeno-jejunal bypass with/without sleeve gastrectomy, distal rygb (common channel ≤100 cm).
†† AGB is associated with a high rate of reoperations for complications or conversion to another bariatric procedure for insufficient weight loss in the long term.
‡‡Long-term comparative data are lacking. The effect on nutritional deficiencies remains controversial.
§§ BPD, BPD/DS, or related procedures because are associated with greater nutritional risks related to the increased length of bypassed small intestine.

¶¶ IFSO supports the SADI-S as a recognised bariatric/metabolic procedure, but highly encourages RCT's in the near future.

Evidence tables of individual studies included for clinical effectiveness and safety

[Add here the evidence tables of studies included, include complete references, key characteristics and outcomes.

You may want to differentiate between studies used for the ‘clinical effectiveness’ and the ‘safety’ domain. It is obligatory to use the template tables, but they can be adapted to fit the needs of the assessment team if necessary. k

The SOP on “Data Extraction” in the Companion Guide shall be consulted for further guidance on the process.]

[Please include here the extraction tables with the characteristics, outcomes as defined in the project plan

Table A4: Characteristics of the studies included – RCTs, direct comparison: intervention vs. comparator

Study reference/ID	Sites or regions, countries, time of study	Study type	Intervention (number of randomized patients)	Comparator(s) [number of randomized patients]	Patient population	Primary endpoint; patient-relevant secondary endpoints
Angrisani 2007; Angrisani 2013/ID [28, 29]	Sites/regions: Single site: General and Laparoscopic Surgery Unit, S. Giovanni Bosco Hospital, Naples Country: Italy Time of study: January.2000-November 2000	RCT	RYGB (N = 29)	AGB (N = 30)	Class III obesity	Primary: % weight loss, BMI, reoperations, complications, and comorbidities Secondary: mortality, conversion to an open procedure, postoperative complications leading to reoperation, hospital stay, weight, BMI, decrease in BMI, percentage of excess weight loss, and improvement in co-morbidities
Arceo-Ofaiz 2008; Zarate 2013 [30]	Sites/regions: unclear Country: Mexico Time of study: study initiated in 2003	RCT	RYGB (N = 30)	B-RYGB (N = 30)	Class III obesity	Primary: surgical morbidity, mortality, (weight loss) Secondary: NR

Aasheim 2009; Søvik 2011; Risstad 2015/ID [32]	Sites/regions: 2 sites: Oslo University Hospital, Oslo,and Sahlgrenska University Hospital, Gothenburg, Countries: Norway, Sweden Time of study: 17.03.2006-20.08.2007	RCT	RYGB (N = 31)	DS (N = 29)	Class III obesity, and BMI>50 (super-obesity)	Primary: BMI, Metabolic normalization, Gastro-intestinal side effects Secondary: anthropometric measures, cardiometabolic risk factors, pulmonary function, vitamin status, gastrointestinal symptoms, HR-QoL, and AEs, Health economics, Vitamin/mineral deficiencies, Body composition, Quality of life, Bowel function, Eating pattern
Biter 2020 [230]	Sites/regions: Countries: Netherlands Time of study: 2013-2017?	RCT	RYGB (N=308)	SG(N=315)	Class III obesity	Primary: EWL at 1 year and 2 years postoperatively Secondary: intake of simple carbohydrates at baseline, 1 year and 2 years postoperatively

Capristo 2018 [36]	Sites/regions: Single site: Day Hospital of Obesity and Related Disorders of the Catholic University in Rome Country: Italy Time of study: December 2012 - December 2014	RCT	RYGB (N = 60)	SG (N = 60)	Class III obesity	Primary: Hypoglycemic events (AE), B-cell sensitivity, lipid profile Secondary: changes of body weight, BMI, symptomatic hypoglycemia, lipid profile, insulin sensitivity, insulin secretion during OGTT, abdominal circumferences, body composition 1 year after surgery. Hypoglycemic events during everyday life
Courcoulas 2014; Courcoulas 2015; Courcoulas 2020 reference/ID [37]	Sites/regions: single site; an academic medical center Country: USA Time of study: October 2009 - April 2012	RCT	RYGB (N = 24)	AGB (N = 22)	Class 2 obesity and T2D	Primary: partial and complete DM remission, AEs and death Secondary: diabetes medications and weight change.

Fahmy 2018 [40]	Sites/regions: Single site: Department of Surgery of Kasr El-Ainy Hospital, Cairo University Country: Egypt Time of study: March 2015 - October 2016	RCT	RYGB (N =30)	OAGB (N = 30)	Class III obesity	Primary: weight loss, GERD, biliary reflux, and condition of the stomach and esophagus Secondary: postoperative weight loss and complications, including biliary reflux.
Fink 2020 [41]	Sites/regions: Single site Country: Germany Time of study: The first patient was included in January 2015. The last follow-up visit was conducted in August 2019	RCT	B-SG (N = 47)	SG (N = 47)	Class III obesity and BMI>50 (super-obesity)	Primary: excess weight loss 3 years after surgery Secondary: Type 2 diabetes, insulin use, glycated hemoglobin, Diabetes remission, Quality of life, Reflux symptoms, Regurgitation, Dysphagia, Vitamin D3, B1, B12, Deficiency, weight loss, hiatal hernias, reflux esophagitis

Hedberg 2012 [42]	Sites/regions: Single site, Uppsala Country: Sweden Time of study: f2004 - 2007	RCT	RYGB (N = 23)	BPD-DS (N = 24)	Class III obesity and BMI>50 (super obese)	Primary: BMI reduction Secondary: Excess BMI loss, operative time, morphine consumption, resolution of complications, reoperations, complications
Himpens 2006 reference/ID [46]	Sites/regions: Single site Country: Belgium Time of study: 01.01.2002-31.12. 2002	RCT	AGB (N = 40)	SG (N =40)	Class II obesity	Primary: relative weight loss compared to the ponderal excess before treatment Secondary: hunger sensation, intake of sweets and modifications of GERD

Hofsø 2019 reference/ID [47]	Sites/regions: Single site; Vestfold Hospital Trust (Tønsberg) Country: Norway Time of study: 15.10.2012-01.09.2017	RCT	RYGB (N = 54)	SG (N = 55)	Class III obesity and T2D	Primary: remission of type 2 diabetes, disposition index? Secondary: 1-year changes in glucose homoeostasis, bodyweight, body composition, obesity-related cardiovascular risk factors, and energy balance, obesity-related comorbidities, gastro-oesophagal reflux disease, fatty liver disease, gut microbiota, physical activity, obesity-specific wellbeing, gastrointestinal symptoms, and dietary intake, surgical and medical complications, hypoglycaemic episodes, early and late dumping, and vitamin and mineral deficiencies,

Ignat 2017 reference/ID [48]	Sites/regions: Single site; Department of Digestive and Endocrine Surgery at the University Hospital of Strasbourg Country: France Time of study: unclear	RCT	RYGB (N = 45)	SG (N = 55)	Class III obesity	Primary: EWL, QoL, co-morbidity, AEs, vitamin and glycolipid status. Secondary: improvement in co-morbidity, vitamin and glycolipid status, QoL and AEs.
Karamanakos 2008; Kehagias 2011 reference/ID [50]	Sites/regions: unclear Country: Greece Time of study: January 2005 - February 2007	RCT	RYGB (N = 30)	SG (N = 30)	Class III obesity	Primary: NR Secondary: BMI, excess body weight loss, improvement of obesity related comorbidities, early/late complications

Keidar 2013 reference/ID [52]	Sites/regions: Single site; an obesity clinic Country: Israel Time of study: June 2008 - February 2010	RCT	RYGB (N = 22)	SG (N = 19)	Class? obesity and T2D	Primary: type, effect measure, scales and assessment instruments, endpoints examined Secondary: adverse events

Mingrone 2012; Mingrone 2015 [53]	Sites/regions: Single site: the Day Hospital of Metabolic Diseases and Diabetology of the Catholic University in Rome Country: Italy Time of study: 30.04.2009-31.10.2011	RCT	RYGB (N = 20)	BPD (N = 20)	Class III obesity and BMI, mean kg/m2(SD): RYGB:44.85(5.16); BPD-DS:45.14(7.78)	Primary: rate of diabetes remission Secondary: percentage change of fasting plasma glucose and HbA1c levels, average HbA1c, body-weight, waist-circumference, arterial blood-pressure, plasma cholesterol, HDL-cholesterol and triglycerides, durability of diabetes remission, relapse of hyperglycaemia, overall glycaemic control, changes in bodyweight, BMI, cardiovascular risk, medication use, quality of life, adverse effects of surgery, diabetes related complications, composite endpoint of metabolic control, ADA partial remission at 5 years, ADA complete remission at 5 years

Murphy 2018 [55]	Sites/regions: unclear Country: New Zeeland Time of study: unclear	RCT	SR-RYGB (N = 58)	SG (N = 56)	Class? obesity and T2D BMI, mean kg/m2(SD): SR-RYGB:(); SG:()	Primary: anxiety and depressive symptoms, postoperative complications and mortality (T2D remission weight loss, QOL) Secondary: weight loss, blood pressure, lipid levels, metabolic medication use, quality of life, anxiety and depressive symptoms, adverse events, post-operative complications and mortality
Nguyen 2009; Nguyen 2018 [56, 57]	Sites/regions: Single site; University of California, Irvine Medical Center's bariatric surgery clinic. Country: USA Time of study: 2002 - 2007	RCT	RYGB (N = 111)	AGB (N = 86)	Class III obesity BMI, mean kg/m2(SD): RYGB:47.5(5.5); AGB:45.5(5.4)	Primary: long-term weight loss, morbidity, and changes in comorbidities, QOL Secondary: NR

Paluszkiewicz 2012 [58]	Sites/regions: unclear Country: Poland Time of study: November 2008 - March 2011	RCT	RYGB (N = 36)	SG (N = 36)	Class III obesity BMI, kg/m2: RYGB:48.6(5.4); SG:46.1(5.9)	Primary: complications, weight loss, additional procedures Secondary: Mortality, nutritional deficiencies
Peterli 2014, Peterli 2017 ; Peterli 2018 [59]	Sites/regions: 4 bariatric centres Country: Switzerland Time of study: From January 2007 to November 2011	RCT	RYGB (N = 110)	SG (N = 107)	Class III obesity BMI, mean kg/m2(SD): RYGB:43.6(5.2); SG:44.2(5.3)	Primary: weight loss Secondary: rate of perioperative morbidity and mortality, remission rates of the associated comorbidities, change in quality of life, cost and duration of operation, reoperations, early/late morbidity, change in gastrointestinal hormones

Rasera 2015 [62]	Sites/regions: Single site: the Hospital dos Fornecedores de Cana de Piracicaba (Hospital of Sugarcane Suppliers of Piracicaba), in the State of Sao Paulo Country: Brazil Time of study: June 2010 - October 2011	RCT	RYGB (N = 200)	SR-RYGB (N = 200)	Class? obesity BMI, mean kg/m2(SD): RYGB:47(); SR-RYGB:()	Primary: NR Secondary: NR

Risstad 2016; Svanevik 2015;, Svanevik 2018, Svanevik 2019? [35]	Sites/regions: 2 public tertiary care centers; Oslo University Hospital and Vestfold Hospital Trust Country: Norway Time of study: March 2011- April 2013	RCT	RYGB (N = 61)	D-RYGB (N = 62)	Class III obesity and BMI>50 (super-obesity) BMI, mean kg/m2(SD): RYGB:53.3(2.6); D-RYGB:53.6(3.3)	Primary: change in BMI from baseline until 2 years after surger Secondary: cardiometabolic risk factors, nutritional outcomes, gastrointestinal symptoms, and health-related quality of life, body composition, anthropometry, obesity-related comorbidities, and adverse events including nutritional deficiencies, malabsorption/malnutrition Need for hospital services, Vitamin- and mineral deficiencies

Robert 2019 [63]	Sites/regions: 9 high-volume bariatric institutions in France (Lyon, Saint Etienne, Lille, Saint Grégoire, Paris, Guilherand Gran Country: France Time of study: 13.05.2014–02.03.2016	RCT	RYGB (N = 124)	OAGB (N =129)	Class III obesity BMI, mean kg/m2(SD): RYGB:43.9(5.1); OAGB:43.8(6.1)	Primary: percentage excess BMI loss at 2 years Secondary: weight and BMI, mean length of stay, duration of surgery, quality of life within 2 years of surgery, the incidence of gastro-oesophageal reflux disease and diarrhoea, steatorrhoea at 6 months, dumping syndrome at each follow-up visit, metabolic profile, evaluated by measuring fasting glycaemia, HbA1C, triglycerides, HDL cholesterol, LDL cholesterol, and total cholesterol, antidiabetic, antihypertensive, and lipid-lowering medications, histological modifications of gastric and oesophageal mucosa 2 years after surgery, Diabetes remission, Nutritional status, Malnutrition, vitamin deficiency, anaemia, iron deficiency, serious adverse events, early and late surgical complications

Salminen 2018 [45]	Sites/regions: three tertiary referral hospitals Country: Finland Time of study: April 2008 - June 2010	RCT	RYGB (N = 119)	SG (N = 121)	Class III obesity BMI, mean kg/m2(SD): RYGB:46.4(5.9); SG:45.5(6.2)	Primary: % EWL, resolution of comorbidities, disease specific QOL, remission of diabetes lipids Secondary: Resolution of obesity-related comorbidities, improvement of disease specific QOL, overall morbidity, mortality, lipid disturbances,
Schauer 2012 ; Schauer 2014 ; Schauer 2017 [64]	Sites/regions:, Single site: the Cleveland Clinic Country: USA Time of study: March 2007 - January 2011	RCT	RYGB (N =50)	SG (N = 50)	Class II obesity and T2D	Primary: proportion of patients with a glycated hemoglobin level of 6% or less Secondary: levels of fasting plasma glucose, fasting insulin, lipids, CRP, HOMA-IR index, weight loss, blood pressure, adverse events, coexisting illnesses, changes in medications, nutritional deficiencies,

Seethamaraiah 2017; Shivakumar 2018 [67]	Sites/regions: Single site: the Department of Minimal Access and Bariatric surgery, ILS Hospital, Kolkata Country: India, Time of study: 2013 - 2015	RCT	SG (N = 108)	OAGB (N = 109)	Class III obesity BMI, mean kg/m2(SD): SG:44.57(7.15); OAGB:44.32(7.88)	Primary: percentage of excess weight loss, percentage of actual weight loss, resolution of comorbidities, complications and bariatric analysis reporting and outcome system Secondary: NR
Tognoni 2016 [71]	Sites/regions: single bariatric centre Country: Italy Time of study: January 2014 - January 2015	RCT	SG (N = 25)	B-SG (N = 25)	Class III obesity BMI, mean kg/m2(SD): SG:47.3(6.58); B-SG:44.95(5.85)	Primary: operative time, intraoperative complications, BMI Secondary: differences in operative time, hospital stay, and postoperative short- and long-term complication.

Wallenius 2020 [73]	Sites/regions: two sites: the Sahlgrenska University Hospital, Gothenburg, and Ersta Hospital, Stockholm Country: Sweden Time of study: NR	RCT	RYGB (N = 29)	SG (N = 31)	Class II-III obesity and T2D BMI, mean kg/m2(SD): RYGB:39.5(3.7); SG:40.8(4.1)	Primary: DM remission, HbA1c, weight loss,%EWL, waist circumference Secondary: 30-day surgical complication rates, weight loss, percentage excess weight loss, percentage weight loss, resolution of other co-morbidities associated with obesity and T2D.
Zhang 2015 [74]	Sites/regions: single site; the minimally invasive surgery center, Nankai Hospital. Country: China Time of study: January 2007 - July 2008	RCT	RYGB (N = 32)	SG (N = 32)	Class II obesity BMI, mean kg/m2(SD): RYGB:39.3(3.8); SG:38.5(4.2)	Primary: BMI,%EWL, QOL, Morbidity rate, and resolution or improvement rate of comorbidities Secondary: Postoperative complications, resolution or improvement of comorbidities, and quality of life constitute the secondary endpoint.

a: Primary outcomes contain information without consideration of its relevance for this assessment. Secondary outcomes contain exclusively information on the relevant available outcomes for this assessment

AE: adverse event; N: number of randomized (included) patients; n: relevant subpopulation; RCT: randomized controlled trial; vs.: versus

Characteristics of the studies included: non-RCTs, direct comparison: intervention vs. comparator

No non-RCTs were included in this REA.

Table A5: Inclusion and exclusion criteria

Study reference/ID	Elementary inclusion criteria	Elementary exclusion criteria
Angrisani 2007 [28]	▪ BMI >35 to <50 kg/m2, ▪ Age >16 to <50 years ▪ No hiatal hernia ▪ No previous major abdominal op.	▪ NR
Arceo-Olfaiz 2008 [30]	▪ NR •	▪ NR
Aasheim 2009 [32]	▪ BMI:50–60 ▪ Age 20 to 50 years ▪ Failed to achieve sustained weight loss by non-surgical measures.	▪ Previous bariatric or major abdominal surgery ▪ Severe cardiopulmonary disease ▪ Malignancy ▪ Oral steroid treatment ▪ Drug abuse ▪ Severe psychiatric illness

Biter 2020 [19]	▪ BMI > 40 kg/m2, or BMI >35 kg/m2 with obesity-related comorbidity (such as T2 DM, hypertension, hypercholesterolemia, severe arthrosis and OSAS) for more than 3 years ▪ Age 18 to 60 years ▪ Conservative therapy that has failed or showed only transient results ▪ Completion of psychological screening ▪ Written informed consent ▪ Willingness to conclude the lifelong follow-up programme after surgery.	▪ No informed consent ▪ Psychiatric or psychological disorders ▪ Symptomatic GERD with proton pomp inhibitor use ▪ A diagnosed hiatal hernia with symptoms ▪ Prior bariatric surgery ▪ Prior major abdominal surgery ▪ Inability of reading or understanding the questionnaires ▪ Severe sweet eating.
Capristo 2018 [36]	▪ BMI >40 or 35 to 40 kg/m2 in the presence of obesity complications ▪ Age 25 to 65 years ▪ Ability to understand and comply with the study process.	▪ History of T2D ▪ Previous bariatric surgery ▪ History of medical problems such as mental impairment ▪ Cancer ▪ Major cardiovascular or gastrointestinal or respiratory diseases ▪ Hormonal disorders ▪ Infections ▪ Pregnancy
Courcoulas 2014/TRIABETES [37]	▪ BMI between 30 and 40 kg/m2 ▪ Age 25 to 55 years ▪ For potential subjects with BMI 35 to 40 kg/m2: T2D confirmed by either a documented fasting blood glucose > 126 mg/dl OR treatment with an anti-diabetic medication. ▪ For potential subjects with BMI 30 to 35 kg/m2: T2D that is difficult to control medically and is recommended for the study by the subject's endocrinologist AND treatment with an anti-diabetic medication. Willingness to be randomized to a surgical intervention	▪ Prior bariatric or foregut surgery ▪ Poor overall general health ▪ Impaired mental status, drug and/or alcohol addiction ▪ Currently smoking ▪ Pregnant or plans to become pregnant ▪ Type 1 DM ▪ Portal hypertension and/or Cirrhosis ▪ Failed study-related nutrition or psychological assessment ▪ Current participation in any other research study ▪ Inability to provide informed consent ▪ Unlikely to comply with study protocol ▪ Unable to communicate with study staff ▪ Unable to exercise

Fahmy 2018 [40]	▪ BMI >40 kg/m2 or BMI >35 kg/m2 with comorbidities (hypertension, diabetes mellitus, and osteoarthritis) ▪ Age18 to 59 years. ▪ With documented failure of weight-loss attempts for ≥ 6 months ▪ Good motivation for surgery •	▪ Patients with American Society of Anaesthesiologists score of 4 or higher ▪ Previous obesity or gastric surgery ▪ Hormonal disturbance ▪ Large abdominal ventral hernia ▪ Psychiatric illness
Fink 2020/MISO [41]	▪ BMI ≥35 kg/m2 with relevant obesity-related comorbidities ▪ BMI ≥40 kg/m2. ▪ Age ≥18 to ≤65 years ▪ History of conservative weight-loss treatment failure •	▪ Untreated psychiatric illness ▪ Alcohol or drug abuse ▪ Chronic inflammatory bowel disease ▪ Liver cirrhosis, pregnancy ▪ Expected poor compliance ▪ < 5-year history of malignant disease ▪ Gastroesophageal reflux disease with Barrett oesophagus or hiatal hernias > 5 cm ▪ Patients with previous extensive gastrointestinal or bariatric surgery
Hedberg 2012 [42]	▪ NR	▪ NR
Himpens 2006 [46]	▪ NR only inclusion criteria mentioned are candidates for laparoscopic restrictive operation	▪ NR
Ignat 2017 [48]	▪ BMI from 40 to 60 kg/m2 ▪ Age 18 to 60 years ▪ No contraindication to any of the surgical procedures or to general anaesthesia ▪ No addiction ▪ Patient able to provide informed consent	▪ Patient's preference for a specific procedure ▪ Previous gastrointestinal surgery ▪ Hiatal hernia larger than 2 cm ▪ Psychiatric pathology ▪ Pregnancy ▪ Immunosuppressive treatment ▪ Coagulopathy ▪ Anaemia (haemoglobin level below 10 g/dl) ▪ Malabsorptive disease ▪ Myocardial infarction ▪ Angina ▪ Cardiac failure in the previous year.
Karamanakos 2008 [50]	▪ BMI ≤ 50	▪ Chronic medical or psychiatric illness, substance abuse, and previous gastrointestinal surgery.

Keidar 2008 [52]	▪ BMI > 35 kg/m2 ▪ Age 18 to 65 years ▪ Diagnosis of T2D based on an OGTT performed at baseline with medication discontinued.	▪ Prior gastrointestinal surgery
Mingrone 2012/DIBASY [53]	▪ Age 30 to 60 years ▪ T2D ▪ Duration of diabetes ≥ 5 years ▪ poor glycaemic control (i.e., HbA1c ≥ 7.0%, as confirmed by at least 3 analyses) ▪ Ability to understand and comply with the study protocol	▪ History of type 1 diabetes ▪ Diabetes secondary to a specific disease or glucocorticoid therapy ▪ Previous bariatric surgery ▪ Pregnancy ▪ Other medical conditions requiring short-term hospitalization ▪ Severe diabetes complications ▪ Other severe medical conditions ▪ Geographic inaccessibility
Murphy 2018 [55]	▪ BMI of 35 to 65 kg/m2 ▪ Age 20 to 55 years ▪ T2D diagnosed for at least 6 months ▪ Suitable for either surgical procedure, and committed to follow-up	▪ Postprandial C peptide < 350 pmol/L ▪ Pregnancy ▪ Type 1 diabetes or secondary diabetes ▪ Chronic pancreatitis ▪ Oral steroid therapy ▪ Current smokers ▪ Those not suitable for general anaesthesia.
Nguyen 2009 [56]	▪ BMI 40-60 kg/m2 or 35 kg/m2 with comorbidities ▪ Age 18 to 60 years ▪ Acceptable operative risk ▪ Diagnostic criteria: BMI 40-60	▪ Large ventral hernia ▪ Hiatal hernia ▪ Previous gastric or bariatric surgery
Paluszkiewicz 2012 [58]	▪ BMI ≥40 kg/m2 or ≥ 35kg/m2 with at least one comorbidity (type 2 diabetes, hypertension, dyslipidaemia, obstructive sleep apnea) ▪ Age 18 to 60 years	▪ BMI > 60 ▪ Poorly controlled significant medical or psychiatric disorder ▪ Active alcohol or substance abuse ▪ Active duodenal/gastric ulcer disease ▪ Difficult to treat gastro-oesophageal reflux disease with a large hiatal hernia ▪ Previous major gastrointestinal surgery ▪ Diagnosed or suspected malignancy

Peterli 2014/SMBOSS [59]	▪ BMI >40 or >35 kg/m2 with presence of at least 1 comorbidity ▪ Age 18 to 65 years ▪ Failure of conservative treatment over 2 years	▪ Severe symptomatic GERD despite medication ▪ Large hiatal hernia ▪ Expected dense adhesions at the level of the small bowel ▪ Need for endoscopic follow-up of the duodenum ▪ Patients with inflammatory bowel disease ▪ General contraindications for major abdominal surgery
Rasera 2016 [62]	▪ BMI of 35 kg/m2 and higher ▪ Age 18 to 65 years; both genders ▪ Scheduled for gastric bypass surgery ▪ Agreed on the randomized and confidentiality standards	▪ Pregnancy or consumptive
Robert 2019/YOMEGA [63]	▪ BMI ≥ 40 kg/m² or BMI ≥ 35 kg/m² associated with one or more co-morbidities (type 2 diabetes, arterial hypertension, sleep apnea, dyslipidaemias, arthritis) ▪ Age18 to 65 years ▪ Benefited from an upper GI endoscopy with biopsies, from a pluridisciplinary evaluation, with a favourable opinion for a gastric bypass ▪ Understands and accepts the need for a long term follow-up ▪ Agrees to be included in the study and signs the informed consent form ▪ Affiliated to a healthcare insurance plan	▪ History of esophagitis on upper GI endoscopy ▪ Patient with severe gastroesophageal reflux disease ▪ Resistant to medical treatment ▪ Presence of dysplastic modifications of the gastric mucosa or a history of gastric cancer ▪ Upper gastrointestinal endoscopy.
Salminen 2018 [45]	▪ BMI greater than 40 or greater than 35 with a significant obesity-associated comorbidity ▪ Age 18 to 60 years ▪ Previous failed adequate conservative treatment.	▪ BMI greater than 60 ▪ Significant psychiatric or eating disorder ▪ Active alcohol or substance abuse ▪ Active gastric ulcer disease ▪ Severe gastroesophageal reflux with a large hiatal hernia ▪ Previous bariatric surgery.
Schauer 2012/STAMPEDE [64]	▪ BMI of 27 to 43 ▪ Age 20 to 60 years ▪ Diagnosis of type 2 diabetes (glycated haemoglobin level, >7.0%)	▪ Previous bariatric surgery ▪ Other complex abdominal surgery ▪ Poorly controlled medical or psychiatric disorders.

Seethamaraiah 2017 [67]	▪ BMI > 35 kg/m2 and less than 60 kg/m2 ▪ Age 18 to 60 years	▪ History of psychiatric illness ▪ Pregnancy ▪ Previous bariatric surgery, non-compliant ▪ Non-willing to be part of the RCT ▪ Lost for follow-up
Svanevik 2015 [35]	▪ BMI 50 to 60 kg/m2 at the time of referral ▪ BMI 48 to 62 kg/m2 at enrollment ▪ Age 20 to 60 years.	▪ Previous bariatric or major abdominal surgery ▪ Urolithiasis ▪ Chronic liver disease ▪ Conditions associated with poor compliance ▪ Severe somatic illness ▪ Psychiatric diseases ▪ Substance abuse
Tognoni 2013 [71]	▪ NR	▪ Age <18 or >60 years ▪ Previous bariatric or gastrointestinal surgery ▪ Psychiatric illness ▪ Pregnancy ▪ Absolute contraindications to pneumoperitoneum
Wallenius 2020/CONTROL [73]	▪ BMI between 35 and 50 kg/m2 ▪ Age18 to 60 years ▪ T2D requiring antidiabetic medications	▪ Uncontrolled psychiatric disorder ▪ Alcohol and/or substance abuse ▪ Severe nephropathy (chronic kidney disease index >2) ▪ Retinopathy or neuropathy ▪ Previously undergone surgical weight reducing procedures ▪ If Barrett's oesophagus was diagnosed on preoperative endoscopy.
Zhang 2014 [74]	▪ BMI > 32 to <50 kg/m2 ▪ Age >16 to <60 years ▪ Absence of chronic medical or psychiatric illness ▪ Substance abuse ▪ Previous gastrointestinal surgery ▪ Willingness to accept randomized allocation to LSG or LRYGB	▪ NR

Table A6: Characterisation of the interventions – RCT, direct comparision: intervension vs. comparator

Study	Intervention. Bariatric procedure	Comparator. Another Bariatric Procedure
Angrisani 2007	AGB. Dietician counselling every 3 months for the first year and every 6 months for subsequent years.	RYGB.Dietician counselling every 3 months for the first year and every 6 months for subsequent years. Bypass patients were instructed to take postoperative supplements (vitamin B12 1000 mg, vitamin A 10,000 UI, and vitamin D 50,000 UI IM monthly; oral multivitamin, iron and calcium, carbonate 1500 mg PO daily) for all of their life
Arceo-Olfaiz 2008	B-RYGB. All patients had undergone standard nutritional and psychological counselling before and after surgery.	RYGB. All patients had undergone standard nutritional and psychological counselling before and after surgery.
Aasheim 2009	BPD-DS. A standard regimen of vitamin and mineral supplementation was prescribed	RYGB. A standard regimen of vitamin and mineral supplementation was prescribed
Biter 2020	*SG.No further treatment reported.*	*RYGB.No further treatment reported.*
Capristo 2018	SG. Patients were evaluated by a multidisciplinary team (including endocrinologists, surgeons, dietitians, and nurses) at baseline and at 1,3,6,9, and 12 months	RYGB. Patients were evaluated by a multidisciplinary team (including endocrinologists, surgeons, dietitians, and nurses) at baseline and at 1,3,6,9, and 12 months
Courcoulas 2014/TRIABETES	AGB. Modest energy restriction, physical activity, and behavioural	RYGB. Modest energy restriction, physical activity, and behavioural counselling

	counselling	
Fahmy 2018	OAGB. Patients were advised to take a daily multivitamin tablet as a supplement, calcium supplement, and vitamin B12 injection. Patients were operated upon after following a 2-week low calorie diet.	RYGB. Patients were advised to take a daily multivitamin tablet as a supplement, calcium supplement, and vitamin B12 injection Patients were operated upon after following a 2-week low calorie diet.
Fink 2020/MISO	*B-SG. No further treatment reported.*	*SG. No further treatment reported.*
Hedberg 2012	BPD-DS. Supplementation with multivitamin (iron 15 mg. calcium 240 mg, vitamin A 600 µg, vitamin D3 750 µg, and vitamin E 60 mg) and vitamin B12. Followed up by a dietician at 3, 6, and 12 months and internist al 6 and 12 months,	RYGB. Supplementation with multivitamin (iron 15 mg. calcium 240 mg, vitamin A 600 µg, vitamin D3 750 µg, and vitamin E 60 mg) and vitamin B12. Followed up by a dietician at 3, 6, and 12 months and internist al 6 and 12 months,
Himpens 2006	*AGB. No further treatment reported*	*SG. No further treatment reported.*
Ignat 2017	*SG. No further treatment reported*	*RYGB. No further treatment reported*
Karamanakos 2008	*SG. No further treatment reported*	*RYGB. No further treatment reported*
Keidar 2008	*SG. No further treatment reported*	*SG. No further treatment reported*
Mingrone	*BPD. No further treatment reported*	*RYGB. No further treatment reported*

2012/DIBASY		
Murphy 2018	*B-RYGB. No further treatment reported*	*RYGB. No further treatment reported*
Nguyen 2007	AGB. Regular adjustment at the clinic.	*RYGB. No further treatment reported*
Paluszkiewicz 2012	SG. The patients received a clear liquid diet after correct UGI for 3-6 days. They continued with a pureed diet for the next 2-3 weeks. Postoperatively, one tablet of multivitamin and mineral supplements and sublingual iron at a dose of 0.1 g daily were prescribed. Vitamin B12 supplementation was given sublingually every month at a dose of 1000 µg	RYGB (open). The patients received a clear liquid diet after correct UGI for 3-6 days. They continued with a pureed diet for the next 2-3 weeks. Postoperatively, one tablet of multivitamin and mineral supplements and sublingual iron at a dose of 0.1 g daily were prescribed. Vitamin B12 supplementation was given sublingually every month at a dose of 1000 µg
Peterli 2014/SMBOSS	*SG. No further treatment reported*	*RYGB. No further treatment reported*
Rasera 2016	B-RYGB. A pureed diet started from the twentieth postoperative day and the solid food diet started on the thirtieth postoperative day, as well as a single multivitamin tablet daily routine.	RYGB. A pureed diet started from the twentieth postoperative day and the solid food diet started on the thirtieth postoperative day, as well as a single multivitamin tablet daily routine.
Robert	OAGB. A systematic supplementation	RYGB. A systematic supplementation of

2019/YOMEGA	of multivitamins, iron, calcium, vitamin B12, and vitamin D was prescribed associated with 40 mg of proton-pump inhibitor and 500 mg of ursodeoxycholic acid for the first 6 months after surgery	multivitamins, iron, calcium, vitamin B12, and vitamin D was prescribed associated with 40 mg of proton-pump inhibitor and 500 mg of ursodeoxycholic acid for the first 6 months after surgery
Salminen 2018	*SG. No further treatment reported.*	*RYGB. No further treatment reported.*
Schauer 2012/STAMPEDE	SG. Daily supplemental multivitamins, vitamin B12, vitamin D, calcium, and iron.	RYGB. Daily supplemental multivitamins, vitamin B12, vitamin D, calcium, and iron.
Seethamaraiah 2017	*OAGB. No further treatment reported.*	*SG. No further treatment reported.*
Svanevik 2015	D-RYGB. Participants were advised to consume liquids only during the first postoperative week, to adhere to a semiliquid diet during the second week, and to gradually introduce normal food to their diet during the third week after surgery. Low molecular weight heparin was administered subcutaneously the first 10 days after surgery, and all patients were recommended a standard daily oral supplement of a multivitamin and mineral tablet, iron, calcium, and vitamin D. Vitamin B12 was administered through injections, and	RYGB. Participants were advised to consume liquids only during the first postoperative week, to adhere to a semiliquid diet during the second week, and to gradually introduce normal food to their diet during the third week after surgery. Low molecular weight heparin was administered subcutaneously the first 10 days after surgery, and all patients were recommended a standard daily oral supplement of a multivitamin and mineral tablet, iron, calcium, and vitamin D. Vitamin B12 was administered through injections, and ursodeoxycholic acid prescribed for 6 months in order to prevent gallstone formation.

	ursodeoxycholic acid prescribed for 6 months in order to prevent gallstone formation.	
Tognoni 2013	B-SG. Alimentary advices included a diet consisting of clear liquids and pureed foods for 15 days and a semisolid diet for the next 15 days. After the first 30 days, patients gradually began a low-fat, low-carbohydrate, high-protein solid diet based on the advice of a dietitian.	SG. Alimentary advices included a diet consisting of clear liquids and pureed foods for 15 days and a semisolid diet for the next 15 days. After the first 30 days, patients gradually began a low-fat, low-carbohydrate, high-protein solid diet based on the advice of a dietitian.
Wallenius 2020/CONTROL	SG. A standardized supplementation regimen of micronutrients was prescribed to all patients including daily intake of 100 to 200 mg iron, 1 g calcium, 800 to 1600 U of vitamin D3, 1 mg vitamin B12, and a multivitamin supplementation. Advised to reduce their antidiabetic medications after the operation and to contact their general practitioner for further adjustment of medications. 20 mg omeprazole was given daily for 2 months starting immediately after the operation	RYGB.A standardized supplementation regimen of micronutrients was prescribed to all patients including daily intake of 100 to 200 mg iron, 1 g calcium, 800 to 1600 U of vitamin D3, 1 mg vitamin B12, and a multivitamin supplementation. Advised to reduce their antidiabetic medications after the operation and to contact their general practitioner for further adjustment of medications.
Zhang 2014	SG. Received multivitamins and mineral supplementation daily, for 6	RYGB. Received multivitamins and mineral supplementation daily, for their remaining

months.	lifetime.

AGB. Adjustable Gastric Banding; B-RYGB. Banded RYGB; B-SG. Banded SG; BPD. Biliopancreatic diversion; BPD-DS. Biliopancreatic diversion with duodenal switch; D-RYGB. Distal RYGB; OAGB. One Anastomosis Gastri Bypass; RYGB. Roux-en-Y Gastric Bypass; SG. Sleeve gastrectomy

Table A7: Baseline characteristics of the study populations – RCT, direct comparison: intervention vs. Comparator

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Angrisani 2007; Angrisani 2013	RYGB N[a] =29	AGB N[a] =30
Age [years], mean (SD)	34.1 (8,9)	33,8 (9,1)
Gender, [f], n (%)	20 (83)	22 (81)
Weight [kg], mean (SD)	118,2 (13,2)	117,1 (12,8)
BMI [kg/m^2], mean (SD)	43,8 (4,1)	43,4 (4,2)
Obesity class	3	3
Race/Ethnicity [white], n (%):	NR	NR
Socioeconomic status	NR	NR
Comorbidities:		

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
T2D, n (%): Duration of diabetes, mean no of years (SD) Hypertension, n (%) Dyslipidemia, n (%) Sleep apnea, n (%) Joint disease, n (%) Metabolic syndrome, n (%) GERD, n (%)	1 (4,2) NR 1 (4,2) 2 (8,3) 0 (0) NR NR NR	0 (0) NR 3 (11,1) 0 (0) 1 (3,7) NR NR NR
Study reference/ID: Aasheim 2009; Søvik 2010, 2011, 2012, Risstad 2015	RYGB N[a] = 31	BPD-DS N[a] = 29
Age [years], mean (SD) Gender no females (%) Weight, mean (SD) BMI, kg/m2t, mean (SD)	35,2 (7,8) 23 (74) 162 (24,1) 54,8 (3,2)	36,1 (5,26) 19 (66) 162 (19,7) 55,2 (3,49)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Obesity class:	3	3
Race/Ethnicity, no (%) white:	33 (97)	27 (93)
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D:, no (%):	5 (16)	6 (21)
-Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%)::::	8 (25,8)	8 (27,5)
Dyslipidemia no (%)::::	24 (77)	24 (83)
Sleep anea no (%)::	5 (16)	6 (21)
Joint disease no (%):	NR	NR
Metabolic síndrome no (%)::	20 (65)	23 (79)
GERD no (%)::	5 (16)	4 (13,8)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Study reference/ID: Biter 2020	RYGB N[a] = 308	SG N[a] = 315
Age [years], mean (SD)	43 (11)	43 (10)
Gender no females (%)	256 (83,1)	252 (80,0)
Weight, mean (SD)	NR	NR
BMI, kg/m2t, mean (SD)	43,4 (4,7)	43,6 (4,7)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D:, no (%):	57 (18,5)	64 (20,4)
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%)::::	NR	NR
Dyslipidemia no (%)::::	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Sleep anea no (%)::	NR	NR
Joint disease no (%):	NR	NR
Metabolic síndrome no (%)::	NR	NR
GERD no (%)::	NR	NR
Study reference/ID: Capristo 2018	RYGB N[a] = 60	SG N[a] = 60
Age [years], mean (SD)	45,76 (9,68)	43,07 (9,17)
Gender no females (%)	NR	NR
Weight, mean (SD)	121,57 (18,32)	124,19 (13,3)
BMI, kg/m2t, mean (SD)	43,44 (4,25)	43,1 (3,96)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Comorbidities, n (%)		
T2D:, no (%):	0 (0)	0 (0)
Duration of diabetes, mean no of years (SD):	NA	NA
Hypertension no (%)::::	NR	NR
Dyslipidemia no (%)::::	NR	NR
Sleep anea no (%)::	NR	NR
Joint disease no (%):	NR	NR
Metabolic síndrome no (%)::	NR	NR
GERD no (%):	NR	NR
Study reference/ID: Courcoulas 2012; 2015; 2020	RYGB N[a] = 24	LAGB N[a] = 22
Age [years], mean (SD)	46,3/7,2)	47,3 (7)
Gender no females (%)	19/79,2)	18 (81,8)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Weight, mean (SD)	99,8 (12,8)	99,5 (14,1)
BMI, kg/m2t, mean (SD)	35,5 (2,6)	35,5 (3,4)
Obesity class:	2	2
Race/Ethnicity, no (%) white:	16/66,7)	19 (86,4)
Socioeconomic status		
Comorbidities, n (%)		
T2D: no (%):	24 (100)	22 (100)
Duration of diabetes, mean no of years (SD):	7,4 (4,5)	6,1 (4,3)
Hypertension no (%)::::	12 (50)	13 (59,1)
Dyslipidemia no (%)::::	14 (58,1)	16 (72,7)
Sleep anea no (%)::	NR	NR
Joint disease no (%):	NR	NR
Metabolic síndrome no (%)::	NR	NR
GERD no (%)::	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Study reference/ID: Fahmy 2018	RYGB N[a] = 30	OAGB N[a] = 30
Age [years], mean (SD)	32,7 (7,3)	31,3 (8)
Gender no females (%)	NA	54 (90)
Weight, mean (SD)	126,7 (16,6)	127,7 (22,9)
BMI, kg/m2t, mean (SD)	44,1 (4,7)	45,5 (5,3)
Obesity class:		
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D: no (%):	8 (26,8)	9 (30)
Duration of diabete, mean no of years s (SD):	NR	NR
Hypertension no (%):	4 (13,3)	6 (20)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic syndrome no (%)::	NR	NR
GERD no (%)::	NR	NR
Study reference/ID: Fink 2020	B-SG N[a] = 47	SG N[a] = 47
Age [years], mean (SD)	43,4	40,9
Gender no females (%)	35 (74,5)	31 (66)
Weight, mean (SD)	147	147,5
BMI, kg/m2t, mean (SD)	51	50,7
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Comorbidities, n (%)		
T2D: no (%):	11 (23,4)	6 (12,8)
Duration of diabetes, mean no of years (SD):	3	3
Hypertension no (%):	26 (53,3)	20 (42,6)
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic syndrome no (%)::	NR	NR
GERD no (%):	7 (14,9)	7 (14,9)
Study reference/ID: Hedberg 2012	RYGB N[a] = 23	BPD-DS N[a] = 24
Age [years], mean (SD)	37,9 (10,4)	40,2 (9,5)
Gender no females (%)	10 (43,5)	12 (50)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Weight, mean (SD)	NR	NR
BMI, kg/m2t, mean (SD)	54,5 (5,6)	54,5 (6,7)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D: no (%):	1 (4,3)	6 (25)
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	7 (30,4)	6 (25)
Dyslipidemia no (%):	0	0
Sleep anea no (%):	3 (13)	4 (16,6)
Joint disease no (%):	NR	NR
Metabolic syndrome no (%):	NR	NR
GERD no (%)::	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Study reference/ID: Hofsø 2019	RYGB N[a] =54	SG N[a] = 55
Age [years], mean (SD)	48,2 (8,9)	47,1 (10,2)
Gender no females (%)	40 (74)	32 (68)
Weight, mean (SD)	124,4 (23,2)	126,7 (21,4)
BMI, kg/m2t, mean (SD)	42,4 (5,4)	42,1 (5,3)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	51 (94)	53 (96)
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D: no (%):	54 (100)	55 (100)
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Dyslipidemia no (%): Sleep anea no (%): Joint disease no (%): Metabolic syndrome no (%):: GERD no (%):	NR NR NR NR NR	NR NR NR NR NR
Study reference/ID: Himpens 2006	AGB N[a] = 40	SG N[a] = 40
Age [years], mean (SD) Gender no females (%) Weight, mean (SD) BMI, kg/m2t, mean (SD) Obesity class: Race/Ethnicity, no (%) white: Socioeconomic status	36 33 (82,5) NR 37 2 NR NR	40 31 (77,5) NR 39 2 NR NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Comorbidities, n (%)		
T2D, no (%):	NR	NR
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	NR	NR
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic syndrome no (%)::	NR	NR
GERD no (%):	6 (15)	8 (20)
Study reference/ID: Ignat 2017	RYGB N[a] = 45	SG N[a] = 55
Age [years], mean (SD)	35,2 (9,4)	35,1 (9,7)
Gender no females (%)	39 (86,7)	43 (78,2)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Weight, mean (SD)	129,5 (21,2)	128,6 (18,3)
BMI, kg/m2t, mean (SD)	47 (5,6)	45,5 (4.8)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D, no (%):	NR	NR
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	NR	NR
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic syndrome no (%)::	NR	NR
GERD, no (%):	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Study reference/ID: Kehagias 2011	RYGB N[a] = 30	SG N[a] = 30
Age [years], mean (SD)	36 (8,4)	33,7 (9,9)
Gender no females (%)	22 (73,3)	22 (73,3)
Weight, mean (SD)	123,1 (13,9)	126,9 (18)
BMI, kg/m2t, mean (SD)	45,8 (3,7)	44,9 (3,9)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D, no (%):	5 (16,6)	1 (4,3)
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	5 (16,6)	4 (13,3)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Dyslipidemia no (%): Sleep anea no (%): Joint disease no (%): Metabolic síndrome no (%): GERD no (%):::	NR 3 (10) 6 (20) NR 5 (16,6)	NR 6 (20) 5 (16,7) NR 2 (6,6)
Study reference/ID: Keidar 2013	RYGB N[a] = 22	SG N[a] = 19
Age [years], mean (SD) Gender no females (%) Weight, mean (SD) BMI, kg/m2t, mean (SD) Obesity class: Race/Ethnicity, no (%) white: Socioeconomic status	51,45 (8,3) 8 (36,4) 118,04 (16,5) 42 (4,8) 3 NR NR	47,7 (11,7) 9 (47,4) 117,9 (17,8) 42,5 (5,2) 3 NR NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Comorbidities, n (%)		
T2D no (%):	19 (100)	18 (100)
Duration of diabetes, mean no of years (SD):	5 (5,5)	6,7 (5,3)
Hypertension no (%):	NR	NR
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic syndrome no (%)::	NR	NR
GERD no (%):	NR	NR
Study reference/ID: Mingrone 2012, and 2015	RYGB N[a] = 20	BPD-SG N[a] = 20
Age [years], mean (SD)	43,9 (7,57)	42,75 (8,06)
Gender no females (%)	12 (60)	10 (50)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Weight, mean (SD)	129,84 (22,58)	137,85 (30,35)
BMI, kg/m2t, mean (SD)	44,85 (5,16)	45,14 (7,78)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	20 (100)	20 (100)
Duration of diabetes, mean no of years (SD):	6,03 (1,18)	6 (1,26)
Hypertension no (%):	NR	NR
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic síndrome no (%):	NR	NR
GERD no (%):	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Study reference/ID: Murphy 2018	SR-RYGB N[a] = 58	SG N[a] = 56
Age [years], mean (SD)	46,6 (6,7)	45,5 (6,4)
Gender no females (%)	33 (59)	26 (45)
Weight, mean (SD)	123,4 (21,3)	126,7 (24,5)
BMI, kg/m2t, mean (SD)	NR for whole group	NR for whole group
Obesity class:	NA	NA
Race/Ethnicity, no (%) white:	34 (61)	38 (66)
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	58 (100)	56 (100)
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic syndrome no (%):	NR	NR
GERD no (%):	NR	NR
Study reference/ID: Nguyen 2009 and 2018	RYGB N[a] = 111	AGB N[a] = 86
Age [years], mean (SD)	41,4 (11)	45,8 (9,8)
Gender no females (%)	86 (77,4)	65 (75,6)
Weight, mean (SD)	132,9 (21,3)	129,3 (20,9)
BMI, kg/m2t, mean (SD)	47,5 (5,5)	45,5 (5,4)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Comorbidities, n (%)		
T2D no (%):	23 (20,7)	23 (26,7)
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	43 (38,7)	44 (51,5)
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic síndrome no (%):	NR	NR
GERD no (%):	NR	NR
Study reference/ID: Peterli papers	RYGB N[a] = 100	SG N[a] = 107
Age [years], mean (SD)	42,1 (11,2)	43 (11,1)
Gender no females (%)	79 (71,8)	77 (72)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Weight, mean (SD)	124,8 (19,8)	123,5 (19,4)
BMI, kg/m2t, mean (SD)	44,2 (5,3)	43,5 (5,2)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	28 (25,5)	26 (23,3)
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	65 (59,1)	67 (62,6)
Dyslipidemia no (%):	56 (50,9)	72 (67,3)
Sleep anea no (%):	46 (41,8)	51 (47.7)
Joint disease no (%):	NR	NR
Metabolic syndrome no (%):	NR	NR
GERD no (%):	51 (46,4)	47 (43,9)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Study reference/ID: Rasera 2016	RYGB N[a] = 200	SR-RYGB N[a] = 200
Age [years], mean (SD)	36	NA
Gender no females (%)	NR (94,1)	NR (86,5)
Weight, mean (SD)	125	NA
BMI, kg/m2t, mean (SD)	47	NA
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR (73)	NR (79)
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	NR	NR
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Dyslipidemia no (%): Sleep anea no (%): Joint disease no (%): Metabolic syndrome no (%): GERD no (%):	NR NR NR NR NR	NR NR NR NR NR
Study reference/ID: Risstad 2016, Svanevik 2015, 2018 and 2019	RYGB N[a] = 61	D-RYGB N[a] = 62
Age [years], mean (SD) Gender no females (%) Weight, mean (SD) BMI, kg/m2t, mean (SD) Obesity class: Race/Ethnicity, no (%) white: Socioeconomic status	39,4 (9,3) 36 (63) 160.2 (19,9) 53,3 (2,6) 3 57 (100) NR	42 (8,2) 37 (66) 157.4 (17,3) 53,6 (3,3) 3 55 (98) NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Comorbidities, n (%)		
T2D no (%):	14 (25)	19 (34)
Duration of diabetes, mean no of years (SD):	4.0	2,5
Hypertension no (%):	33 (58)	34 (61)
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	21 (36)	19 (34)
Joint disease no (%):	NR	NR
Metabolic syndrome no (%):	47 (82,5)	51 (91,1)
GERD no (%):	14 (25)	16 (29)
Study reference/ID: Robert 2019	RYGB N[a] = 124	OAGB N[a] = 129
Age [years], mean (SD)	42,5 (10,2)	44,4 (11,4)
Gender no females (%)	91 (78)	85 (73)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Weight, mean (SD)	119,9 (18,7)	121,2 (24,4)
BMI, kg/m2t, mean (SD)	43,9 (5,1)	43,8 (6,1)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	58 (27)	30 (29)
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	71 (31)	33 (28)
Dyslipidemia no (%):	42 (18)	20 (17)
Sleep anea no (%):	128 (56)	68 (59)
Joint disease no (%):	NR	NR
Metabolic syndrome no (%):	NR	NR
GERD no (%):	NR	NR

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Study reference/ID: Salminen 2018	RYGB N[a] = 119	SG N[a] = 121
Age [years], mean (SD)	48,4 (9,3)	48,5 (9,6)
Gender no females (%)	80 (67,2)	87 (71,9)
Weight, mean (SD)	134,9 (22,5)	130,1 (21,5)
BMI, kg/m2t, mean (SD)	46,4 (5,9)	45,5 (6,2)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	NR	NR
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	87 (73,1)	83 (68,6)

Study reference/ID **Characteristics** **Category**	**Intervention**	**Comparator**
Dyslipidemia no (%):	45 (37,8)	39 (37,2)
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic syndrome no (%):	NR	NR
GERD no (%):	NR	NR

Study reference/ID: Schauer 2012, 2014; 2017	RYGB N[a] = 50	SG N[a] = 50
Age [years], mean (SD)	48,3 (8,4)	47,9 (8)
Gender no females (%)	29 (58)	39 (78)
Weight, mean (SD)	106,7 (14,8)	100,8 (16,4)
BMI, kg/m2t, mean (SD)	37 (3,3)	36,2 (3,9)
Obesity class:	2	2

Race/Ethnicity, no (%) white:	37 (74)	36 (72)
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	50 (100)	50 (100)
Duration of diabetes, mean no of years (SD):	8,2 (5,5)	8,5 (4,8)
Hypertension no (%):	35 (70)	30 (60)
Dyslipidemia no (%):	44 (88)	40 (80)
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic syndrome no (%):	45 (90)	47 (94)
GERD no (%):	NR	NR
Study reference/ID: Shivakumar 2018	SG N[a] = 108	SG N[a] = 109
Age [years], mean (SD)	39,89 (11,75)	42,89 (14,02)
Gender no females (%)	65 (65)	62 (61)
Weight, mean (SD)	117,64 (25,97)	114,39 (22,5)

BMI, kg/m2t, mean (SD)	44,47 (7,15)	44,32 (7,88)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	47 (47)	49 (49)
-Duration of diabetes (SD):	NR	NR
Hypertension no (%):	56 (56)	53 (53)
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	18 (18)	24 (24)
Joint disease no (%):	32(32)	26 (26)
Metabolic syndrome no (%):	NR	NR
GERD no (%):	NR	NR
Study reference/ID: Paluszkiewicz 2012	RYGB N[a] = 36	SG N[a] = 36
Age [years], mean (SD)	43,9 (10,8)	44,9 (10,6)
Gender no females (%)	23 (63,9)	26 (72,2)

Weight, mean (SD)	137,7 (17,7)	130,7 (15,5)
BMI, kg/m2t, mean (SD)	48,6 (5,4)	46,1 (5,9)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	14 (38,9)	10 (27,8)
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	30 (83,3)	25 (69,4)
Dyslipidemia no (%):	31 (86,1)	31 (86,1)
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic syndrome no (%):	NR	NR
GERD no (%):	NR	NR

Study reference/ID: Tognoni 2013	SG N[a] = 25	B-SG N[a] = 25
Age [years], mean (SD)	43,7 (9,8)	45,7 (12,7)
Gender no females (%)	16 (64)	16 (64)
Weight, mean (SD)	NR	NR
BMI, kg/m2t, mean (SD)	47,3 (6,58)	44,95 (5,85)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	7 (28)	5 (20)
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	14 (56)	7 (28)
Dyslipidemia no (%):	NR	NR
Sleep anea no (%):	6 (28)	2 (8)
Joint disease no (%):	NR	NR
Metabolic síndrome no (%):	NR	NR
GERD no (%):	NR	NR

Study reference/ID: Wallenius 2020	RYGB N[a] = 25	SG N[a] = 24
Age [years], mean (SD)	49,1 (9,2)	47 (10,7)
Gender no females (%)	12 (48)	11 (45,8)
Weight, mean (SD)	119 (15,4)	120 (19,2)
BMI, kg/m2t, mean (SD)	39,5 (3,7)	40,8 (4,1)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	29 (100)	31 (100)
Duration of diabetes, mean no of years (SD):	5,5 (4,1)	5 (3,7)
Hypertension no (%):	20 (80)	16 (67)
Dyslipidemia no (%):	22 (80)	23 (96)
Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR

Metabolic syndrome no (%):	NR	NR
GERD no (%):	NR	NR
Study reference/ID: Zarate 2013	RYGB N[a] = 30	B-RYGB N[a] = 30
Age [years], mean (SD)	36,5 (9,7)	37,8 (9,6)
Gender no females (%)	26 (87)	27 (90)
Weight, mean (SD)	125 (17)	126,8 (17)
BMI, kg/m2t, mean (SD)	47 (5)	48 (5)
Obesity class:	3	3
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	NR	NR
Duration of diabetes, mean no of years (SD):	NR	NR
Hypertension no (%):	NR	NR
Dyslipidemia no (%):	NR	NR

Sleep anea no (%):	NR	NR
Joint disease no (%):	NR	NR
Metabolic syndrome no (%):	NR	NR
GERD no (%):	NR	NR
Study reference/ID: Zhang 2014	RYGB N[a] = 32	SG N[a] = 32
Age [years], mean (SD)	32,2 (9,2)	29,3 (9,8)
Gender no females (%)	18 (56)	20 (63)
Weight, mean (SD)	NR	NR
BMI, kg/m2t, mean (SD)	39,3 (3,8)	38,5 (4,2)
Obesity class:	2	2
Race/Ethnicity, no (%) white:	NR	NR
Socioeconomic status	NR	NR
Comorbidities, n (%)		
T2D no (%):	8 (25)	9 (28)
Duration of diabetes, mean no of years (SD):	NR	NR

Hypertension no (%):	6 (19)	5 (16)
Dyslipidemia no (%):	13 (41)	13 (41)
Sleep anea no (%):	5 (16)	7 (22)
Joint disease no (%):	4 (13)	2 (6)
Metabolic syndrome no (%):	NR	NR
GERD no (%):	NR	NR

a: Number of randomized patients. Values that are based on other patient numbers are marked in the corresponding line if the deviation is relevant

f: female; m: male; n: number of patients in the category; N: number of patients; ND: no data; RCT: randomized controlled trial; SD: standard deviation; vs.: versus

Table A8: Matrix of outcomes in the included studies/RCTs to be assessed– RCT, direct comparison intervention vs. comparator

Study	Measures of weight change	Diabetes status	HRQOL	Mortality (short– and long term)	Cardiovascular risk reduction	Patient satisfaction with procedure	Adverse events (technical complications e.g. leaks, strictures etc)	Adverse events (reoperations/re-interventions)	Resource use (LOS, readmission to hospital)
Study Angrisani 2007	Y	N	N	Y	Y	N	Y	Y	Y
Study Arceo Olaiz 2008	Y	N	N	Y	N	N	Y	N	N
Study Aasheim 2009	Y	Y	Y	Y	Y	N	Y	Y	Y
Study Biter 2020	Y	N	N	N	N	N	N	N	N
Study Capristo 2018	Y	Y	N	Y	Y	N	Y	Y	Y
Study Courcoulas 2014/TRIABETES	Y	Y	N	Y	Y	N	Y	Y	N
Study Fahmy 2018	Y	N	N	Y	N	N	Y	Y	Y
Study Fink 2020/MISO	Y	Y	Y	Y	Y	N	Y	Y	N
Study Hedberg 2012	Y	N	Y	Y	Y	N	Y	Y	Y

Study Himpens 2006	Y	N	N	Y	N	N	N	N	N
Study Hofsø 2019	Y	Y	N	Y	Y	N	Y	Y	Y
Study Ignat 2017	Y	N	Y	N	N	N	Y	Y	Y
Study Karamanakos 2008	Y	Y	N	Y	Y	N	Y	Y	Y
Study Keidar 2013	Y	Y	N	Y	Y	N	N	N	N
Study Mingrone 2012/DIABASY	Y	Y	N	Y	Y	N	Y	N	N
Study Murphy 2018	Y	Y	Y	Y	Y	N	Y	Y	N
Study Nguyen 2009, 2018	Y	N	Y	Y	Y	N	Y	Y	N
Study Paluszkiewicz 2012	Y	Y	N	Y	Y	N	Y	Y	N
Study Peterli 2014/SMBOSS	Y	Y	Y	Y	Y	N	Y	Y	Y
Study Rasera 2015	Y	N	Y	Y	Y	N	Y	Y	Y
Study Robert 2019/YOMEGA	Y	Y	Y	Y	Y	N	Y	Y	Y
Study Salminen 2018 SLEEVEPASS	Y	Y	Y	Y	Y	N	Y	Y	N

Study Schauer 2012 STAMPEDE	Y	Y	Y	Y	Y	N	Y	Y	N
Study Seethamaraiha 2017	Y	N	Y	Y	Y	N	Y	Y	Y
Study Svanevik 2015	Y	Y	N	Y	Y	N	Y	Y	Y
Study Tognoni 2013	Y	N	N	Y	Y	N	Y	Y	Y
Study Wallenius 2020/CONTROL	Y	Y	N	Y	Y	N	Y	Y	Y
Study Zhang 2014	Y	N	Y	Y	Y	N	Y	Y	Y

Table A9: Summary of results for weight regain following nadir weight after obesity surgery

Author Year	Procedure	No pts.	FU	Nadir	Weight regain (kg)	MD in weight regain (95% CI); (p-value)
AGB vs RYGB						
Angrisani 20071	AGB	30	10 yrs	2 yrs	6.5± (SD) 6.8	-0.30 [-3.93, 3.33]; (p=0.87)
	RYGB	29			6.8 ±(SD) 7.4	
BPD-DS vs RYGB						
Aasheim 2009	BPD-DS	29	5 yrs	1-2 yrs	8.7 (95% CI, 4.8 to 12.5)	-1.20 [-7.98, 5.58]; (p=0.24)

	RYGB	31			9.9 (95% CI, 4.0 to 15.8)	
BPD vs RYGB						
Mingrone 2012 DIBASY	BPD-DS	19	5 yrs	2 yrs	4.56 [5.49]	-1.53 [-4.18, 1.12]; (p=0.24)
	RYGB	19			6.09 [2.51]	
B-SG vs SG						
Fink 2020 MISO	B-SG	47	3 yrs	NR	5.45±6.51	**-5.15 [-7.78, -2.52]**; (p<0.0001)
	SG	47			10.6± 6.51% EWL	
B-RYGB vs. RYGB						
Rasera 2016	SR-RYGB	200	2 yrs	NR	1.1 kg[2]	ND. **Significantly *lower* median weight regain in B-RYGB.**
	RYGB	200	2 yrs	NR	10.5 kg	

AGB: Adjustable Gastric Banding; BPD-DS: Biliopancreatic Diversion with Duodenal Switch; B-SG: Banded Sleeve Gastrectomy; CI: confidence Interval; FU: FollowUp; kg: kilogram; MD: Mean Difference; pts: patients; ND: No Numerical Data; RYGB: Roux-en-Y Gastric Bypass; SR-RYGB: Silicon Ring Roux-en-Y Gastric Bypass

[1]Angrisani also reported regain of BMI units (kg/m2): 3±3 vs 2±1, and EWL% regain10% ± 9 vs 10% ±11

[2]No measure of dispersion provided.

Table A10: Insufficient weight loss at 5 years follow up after obesity surgery; 2 comparisons; 5 studies

Author Year	Procedure	FU	N	n	RR (95% CI)
AGB vs. RYGB (3 studies)					
Angrisani 2007	AGB	5 yrs	30	4	8.71 (0.49, 154.89)
	RYGB		29	0	
Ngiuyen 2009	AGB	5 yrs	88	5	14.16(0.79,252.84
	RYGB		111	0	
Courcoulas 2014 TRIABETES	AGB	5 yrs	20	1	0.80 (0.05, 11.82
	RYGB		16	1	
SG vs. RYGB (2 studies)					
Ignat 2017	SG	5 yrs	55	1	2.48(0.10, 59.07)
	RYGB		45	0	
Peterli 2014 SMBOSS	SG	5 yrs	101	5	2.57(0.51, 12.97)
	RYGB		104	2	

AGB: Adjustable Gastric Banding; CI: Confidence Interval; FU: Follow-up; N: total no of participants; n: no affected by the outcome; RR: Risk Ratio; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve Gastrectomy; yrs: years

Table A11: Results summary for worsening GERD (dichotomous) – RCT direct comparison: 2 comparisons; 2 studies

Study reference/ID	Operationalization	Intervention		Comparator		Intervention vs. Comparator
		N	n(%)	N	n(%)	RR/OR [95% -CI]; (p-value)
SG vs RYGB (1 study)						
Peterli 2014-SMBOSS		SG		RYGB		
	Worsening GERD symptoms at 5 yrs FU.	44	14(31.8)	48	3(6.3)	**5.09(1.57, 16.53)**; (p=0.007)
BPD-DS vs RYGB (1 study)						
Aasheim 2009		BPD-DS		RYGB		
BL: BPD-DS:4/29 (13.8); RYGB:5/31 (16.1)	Worsening GERD symptoms at 5 yrs FU.					Worsening of GERD symptoms in the BPD-DS group, but not in the RYGB group. No numerical data provided.

a: own calculation (csz-method)

BPD-DS: BilioPancreatic Diversion with Duodenal Switch; CI: confidence interval; GERD: Gastro Oesophageal Reflux Disease; N: number of analysed patients; n: number of patients with (at least one) event; ND: no data; RCT: randomized controlled trial; Roux-en-Y Gastric Bypass; RR: relative risk; SG; Sleeve Gastrectomy; vs.: versus; yrs: years

Table A12: Results summary for De Novo GERD (dichotomous) – RCT direct comparison: 2 comparisons; 4 studies

Study	Operationalization	Intervention		Comparator		Intervention vs. Comparator
		N	n(%)	N	n(%)	RR/OR [95% -CI]; (p-value)
AGB vs SG (1 study)						
Himpens 2006		AGB		SG		
	De novo GERD (%) at 1 and 3 yrs FU.		8.8% at 1 yr;20.5% at 3 yrs		21.8% at 1 yr;3.1% at 3 yrs	Significantly greater% of participants with de novo GERD in SG at 1 years, and in AGB at 3 years.
SG vs RYGB (3 studies)						
Peterli 2014-SMBOSS		SG		RYGB		
	De novo GERD at 5 yrs FU.	57	18(31.6)	56	6(10.7)	**2.95 [1.26, 6.88];** (p=0.01)
Schauer 2012-STAMPEDE						
	Assumed de novo GERD (no BL data) at 5 yrs FU.	50	11(22.0)	50	5(10.0)	2.20 [0.82, 5.87]; (p=0.12)
Zhang 2014						
	Assumed de novo GERD (no BL data) at 5 yrs FU.	32	3 (9.4)	32	0 (0)	7.00 [0.38, 130.26]; (p=0.19)

a: own calculation (csz-method): BPD-DS: BilioPancreatic Diversion with Duodenal Switch; CI: confidence interval; GERD: Gastro Oesophageal Reflux Disease; N: number of analysed patients; n: number of patients with (at least one) event; ND: no data; RCT: randomized controlled trial; Roux-en-Y Gastric Bypass; RR: relative risk; SG; Sleeve Gastrectomy; vs.: versus; yrs: years

Table A13: Results summary for severe GERD requiring conversion (dichotomous) – RCT direct comparison: 4 comparison; 6 studies

Study	Operationalization	Intervention		Comparator		Intervention vs. Comparator
		N	n(%)	N	n(%)	RR [95% -CI]; (p-value)
AGB vs RYGB (1 study)						
Angrisani 2007		**AGB**		**RYGB**		
	Conversion due to severe GERD at 10 yrs FU.	27	1(3.7)	24	0 (0)	2.68 [0.11, 62.81]; (p=0.54)
SG vs. RYGB (3 studies)						
		SG		**RYGB**		
Ignat 2017	Conversion due to severe GERD at 5 yrs FU.	37	2 (5.4)	29	0(0)	3.95 [0.20, 79.16]; (p=0.37)
Peterli 2014-SMBOSS	Conversion due to severe GERD at 5 yrs FU.	101	9(8.9)	104	0 (0)	**19.56 [1.15, 331.68**]; (p=0.04)
Salminen 2018 - SLEEVEPASS	Conversion due to severe GERD at 5 yrs FU.	98	7(7.1)	95	0	14.55 [0.84, 251.18]; (p=0.07)
D-RYGB vs RYGB (1 study)						
Svanevik 2015		D-		RYGB		

		RYGB				
BL: D-RYGB:16/62(29); RYGB:14/61 822.9)	Conversion due to severe GERD at 2 yrs FU.					ND. Authors state no differences between groups.
B-SG vs SG (1 study)						
		B-SG		SG		
Fink 2020	Conversion due to severe GERD at 2 yrs FU.	47	2(4.3)	47	1 (2.1)	2.00 [0.19, 21.31]; (p=0.57)

a: own calculation (csz-method)

AGB: Adjustable Gastric Banding; B-SG: Banded Sleeve Gastrectomy; CI: confidence interval; GERD: Gastro Oesophageal Reflux Disease; N: number of analysed patients; n: number of patients with (at least one) event; ND: no data; RCT: randomized controlled trial; Roux-en-Y Gastric Bypass; RR: relative risk; SG: Sleeve Gastrectomy; vs.: versus; yrs: years

Table A14: Results summary for resolution of GERD (dichotomous) – RCT direct comparison: 3 comparisons; 5 studies

Study	**Operationalization**	**Intervention**		**Comparator**		**Intervention vs. Comparator**
		N	**n(%)**	**N**	**n(%)**	**RR [95% -CI]; (p-value)**

AGB vs SG (1 study)						
Himpens 2006		AGB		SG		
	Resolution of GERD at 3 yrs	6	5(83.3)	8	6(75)	1.11 [0.65, 1.90]; (p=0.70)
SG vs RYGB (3 studies)						
Karamanakos 2008		SG		RYGB		
	Resolution of GERD at 3 yrs	2	2(100)	5	5(100)	1.00 [0.57, 1.75]; (p=1.0)
Peterli 2014-SMBOSS		SG		RYGB		
	Resolution of GERD at 5 yrs	44	11	48	29	**0.41 [0.24, 0.72];** (p=0.02)
Zhang 2014		SG		RYGB		
	Resolution of GERD at 5 yrs					All symptoms disappeared after 1 year.
B-SG vs SG (1 study)						
Fink 2020		B-SG		SG		
	Resolution of GERD at 2 yrs	7	3	7	4	0.75 [0.26, 2.18]; (p=0.60)

a: own calculation (csz-method)

AGB: Adjustable Gastric Banding; B-SG: Banded Sleeve Gastrectomy; CI: confidence interval; GERD: Gastro Oesophageal Reflux Disease; N: number of analysed patients;

n: number of patients with (at least one) event; ND: no data; RCT: randomized controlled trial; Roux-en-Y Gastric Bypass; RR: relative risk; SG: Sleeve Gastrectomy; vs.: versus; yrs: years

Table A15: Summary of micronutrient deficiencies and related morbidity: 6 comparisons; 8 studies

Author year	Procedure	N	FU, yrs	Severe anemia/iron deficiency, RR (95%CI)	Protein-calorie malnutrition; RR (95%CI)	Severe vitamin deficiency; RR (95%CI)	Other metabolic complications; RR (95%CI)	Osteoporosis/ osteopenia; RR (95%CI)	Fractures; RR (95%CI)
AGB vs RYGB (2 studies)									
Courcoulas 2014-TRIABETES	AGB	20	5	0					0
	RYGB	16		1(5.5%)					2 (12.5%)
				0.36 [0.02, 8.46]					0.16[0.01; 3.15]; (p=0.23)
Nguyen 2009	AGB	86	10	0					
	RYGB	111		4 (3.6%)					
				0.14 [0.01, 2.62]					
SG vs RYGB (2 studies)									
Ignat 2017	SG	55	5 yrs	2 (3.6%)					
	RYGB	45		7(15.5%)					

				0.23 [0.05, 1.07] P=0.06)					
Schauer 2012-STAMPEDE	SG	49	5 yrs			-		-	6 (12.2%)
	RYGB	48				-		-	4 (8.3%)
									1.47 [0.44, 4.88]; (p=0.53)
D-RYGB vs RYGB (1 study)									
Svanevik 2015	D-RYGB	56	2	3 (5.3%)	3(5.3%)	3(5.3%)			
	RYGB	57		0	1(1.8%)	0			
				7.12 [0.38, 134.81] (p=0.19)	3.05 [0.33, 28.48] (P=0.33)	7.12 [0.38, 134.81]; (p=0.19)			
OAGB vs RYGB (1 study)									
Robert 2019- YOMEGA	OAGB	56	2	1(1.8%)			9 (16.1%)		
	RYGB	49		0			0		
				2.63 [0.11, 63.15] (P=0.55)			**20.09 [1.19, 340.01]**(p=0.04)		

BPD-DS vs RYGB (1 study)									
Aasheim 2009	BPD-DS	29	5	5 (17.2%)	3(10.3%)	2(6.9%)		1(3.4%)	2 (6.9%)
	RYGB	31		1(3.2%)	0	0		0	0
				5.34 [0.66, 43.06] (p=0.12)	7.47 [0.40, 138.58] (p=0.18)	5.33 [0.27, 106.61] (p=0.27)		3.20 [0.14, 75.55]; (p=0.42)	5.33 [0.27, 106.61]; (p=0.27)
BPD vs RYGB (1 study)									
Mingrone 2012-DIBASY	BPD	19	5					3 (15.8%)	
	RYGB	19						1(5.3%)	
								3.00 [0.34, 26.33]; (p=0.32)	

Table A16: Results summary for diabetes remission (dichotomous) – RCTs, direct comparisons: 8 comparisons; 13 studies

Study	**Operationalization**	**Intervention**		**Comparator**		**Intervention vs. Comparator**
		N	**n(%)**	**N**	**n(%)**	**RR [95% -CI]; (p-value)**
AGB vs. RYGB (2 studies)						

		AGB		RYGB		
Angrisani 2007 *Class III obesity. 1 person with T2D, 4.15% DL*	HbA1c <6%; fasting glucose <56 mmol/L), with no medication. FU: at 10 years	0	0 (0)	1	1(100)	-
Courcoulas 2014- TRIABETES *Class II diabetes, and 100% of participants with T2D*	Absence of medications, HbA1c <5.7%, and FPG ≤ 100 mg/d. FU: at 2 years FU: at 5 years	21	6 (28.6)	20	9(45)	0.63 [0.28, 1.46]; (P = 0.28)
		21	4(19)	20	6(30)	0.63 [0.21, 1.92]; (P = 0.42)
SG vs RYGB (5 studies)						
		SG		RYGB		
Karamanakos 2008 Class III obesity; 16.6% T2D; 15% HTN	FPG <126 mg/dL and 2-h plasma glucose <200 mg/dL during OGTT without glycemic therapy. 3 yrs FU.	5	4(80)	5	4(80)	1.00 [0.54, 1.86]; (P = 1.00)
Peterli 2014- SMBOSS Class III obesity; 24.9% T2D; 61% HTN	Remission was defined by the endocrinologist/ physician responsible. FU at 5 years.	26	16(61.5)	28	19(67.8)	0.91 [0.61, 1.35]; (P = 0.63)
Salminen 2018-	HbA1c < 6.0% (42 mmol/mol) and fasting	52	7(13.4)	49	11(22.4)	0.60 [0.25, 1.42]; (P = 0.25)

SLEEVEPASS Class III obesity;42.1% T2D; 71% HTN	glucose level less than 100 mg/dL [<5.6 mmol/L] for at least 1 year's duration in the absence of active pharmacologic therapy or ongoing procedures. FU: at 3 years.					
	FU: min benefit at 5 years	52	5(9.6)	49	10(20.4)	0.47 [0.17, 1.28]; (P = 0.14)
	FU: max benefit at 5 years	52	16(30.8)	49	19(38.8)	0.79 [0.46, 1.36]; (P = 0.40)
Schauer 2012- STAMPEDE Class II obesity, 100% T2D, 65% HTN, 84% DL	HbA1c ≤ 6% with no medication. FU: at 3 years. FU: at 5 years	47	10(21.3)	49	17(34.7)	0.61 [0.31, 1.20]; (P = 0.15)
		47	7(14.9)	49	11(22.4)	0.66 [0.28, 1.57]; (P = 0.35)
Wallenius 2020' Class III obesity; 100% T2D; 74% HTN	HbA1c ≤ 6% with no medication. FU at 2 years.	22	12(54.5)	25	12(48)	1.14 [0.65, 1.99]; (P = 0.65)
D-RYGB vs RYGB (1 study)						
		D-RYGB		RYGB		
Svanevik 2015 Class III obesity with BMI>50 (super-obesity);29.5% T2TN; 60% HTN	HbA1c<6.0% and FPG 101mg/dL without glucose-lowering drugs for at least 1 year. FU: at 2 years.	18	12(66.7)	13	9(69.2)	Min benefit: 0.96 [0.59, 1.57]; (P = 0.88)
		18	14(77.8)	13	11(84.6)	Max benefit: 0.92 [0.66, 1.29]; (P = 0.63)

OAGB vs. RYGB (1 study)						
Robert 2019 YOMEGA		OAGB		RYGB		
Class III obesity, 28% T2D,23.5% HTN, and 17.5% DL	HbA1C < 6% (42 mmol/mol), and FPG < 5·6 mmol/L, without active medical therapy or ongoing procedures. FU: at 2 years.	28	12(42.8)	30	6(20)	Min benefit[1] 2.14 [0.93, 4.93]; (P = 0.07)
	FU at 2 years (max benefit)	28	20(71.4)	30	20(66.7)	Max benefit[2] 1.07 [0.76, 1.51]; (P = 0.69)
OAGB vs SG (1 study)						
Seetharamaiah 2017		OAGB		SG		
Class III obesity; 48% T2D, 54.5% HTN	Note: Did not report complete T2D remission; but <6.5 HbA1c without medication	49	43(87.8)	47	37(78.7)	1.11 [0.93, 1.34]; (p=0.24)
BPD/DS vs RYGB (1 study)						
Aasheim 2009		BPD-DS		RYGB		
Class III with super obesity; 18.5% T2D; 26.7% HTN	FPG< 100 mg/dl and at least 1 year without any pharmacological treatment prior to evaluation. FU: at 5 years.	6	6(100)	5	4(80)	1.24 [0.75, 2.05]; (P = 0.41)
BPD vs. RYGB (1 study)						

Mingrone 2012-DIBASY		BPD		RYGB		
Class III diabetes, 100% of participants with T2D	HbA1c ≤ 6% (<42.1 mmol/mol) and FPG <100 mg/dL (5.6 mmol/L) without medication. FU: at 5 years.	19	7(36.8)	19	1(5.3)	7.00 [0.95, 51.54]; (P = 0.06)
B-SG vs. SG (1 study)						
Fink 2020-MISO		BSG		SG		
Class III with super-obesity; 18.1% T2D, 48% HTN	Normal glycemic measurements of at least 1-year duration in absence of antidiabetic medications. FU: at 2 years	11	10(90.9)	6	4(66.7)	Min benefit: 1.36 (0.76, 2.47); (p=0.31)
	FU at 2 years	28	20(71.4)	30	20(66.7)	Max benefit[2]1.07 [0.76, 1.51]; (P = 0.69)

a: own calculation (csz-method); BPD-DS: Bilio-Pancreatic Diversion with Duodenal Switch; B-SG: Banded Sleeve Gastrectomy; DL: DysLipidemia; CI: confidence interval; D-RYGB: Distal Roux-en-y Gastric Bypass; FPG: Fasting Plasma Glucose; FU: Follow-up; HbA1c: glycated haemoglobin; mmol: millimole; HTN: Hypertension; Min: minimum; Max: maximum; N: number of analysed patients; n: number of patients with (at least one) event; ND: no data; OAGB: One Anastomosis Gastric Bypass; OGTT: Oral Glucose Test Tolerance; RCT: randomized controlled trial; RR: relative risk; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve gastrectomy; T2D: Type 2 Diabetes Mellitus; vs.: versus

Table A17: Results summary for hypertension remission (dichotomous) – RCT, 5 comparisons; 8 studies

Study	Operationalization	Intervention		Comparator		Intervention vs. Comparator
		N	n(%)	N	n(%)	RR [95% -CI]; (p-value)

BPD-DS vs. RYGB (1 study)						
Aasheim 2009[1] Class III; BMI>50 (super-obesity); 18.5% T2D; 26.7% HTN	Complete remission of HTN. FU at 5 yrs.	BPD-DS		RYGB		
		8	7(87.5)	8	4(50)	1.75 [0.83, 3.67]; (P = 0.14)
B-SG vs. SG (1 study)						
Fink 2020 MISO Class III; BMI>50 (super-obesity); 18.1% T2D, 48% HTN	Stopped using anti-hypertensive medication. FU at 3 yrs.	B-SG		SG		
		25	16(64)	16	7(43.8)	1.46 [0.78, 2.74]; (P = 0.24)
D-RYGB vs. RYGB (1 study)						
Svanevik 2015 Class III; BMI>50 (super-obesity); 29.5% T2TN; 60% HTN	Remission of HTN. FU at 2 yrs.	D-RYGB		RYGB		
		34	26(77)	34	16(47)	**0.54 [0.35, 0.84]; P=0.006**
SG vs. RYGB (4 studies)						
Karamanakos 2008 Class III obesity; 16.6%	Resolution of HTN: SBP <140 and/or DBP <90 mmHg and no anti-hypertensive drug	SG		RYGB		
		4	3(75)	5	3(60)	1.25 [0.50, 3.11]; (P = 0.63)

T2D; 15% HTN	therapy. FU at 3 yrs					
Peterli 2014-SMBOSS Class III obesity; 24.9% T2D; 61% HTN	Remission of HTN: no symptoms and/or no medication. FU at 5 yrs.	SG		RYGB		
		64	40(62.5)	64	45(70.3)	0.89 [0.69, 1.14]; (P = 0.35)
Salminen 2018-SLEEVEPASS Class III obesity; 42.1% T2D; 71% HTN	Stopped using anti-hypertensive medication. FU at 5 yrs.	SG		RYGB		
		73	37(50.7)	68	20(29.4)	**1.72 [1.12, 2.65];** (P = 0.01)
Wallenius 2020 CONTROL Class III obesity; 100% T2D; 74% HTN	Complete remission of HTN. FU at 2 years.	SG		RYGB		
		16	0(0)	20	1(5.0)	0.41 [0.02, 9.48]; (P = 0.58)
OAGB vs. SG (1 study)						
Seetharamaiah 2017* Class III obesity; 48% T2D, 54% HTN	Remission of HTN. FU at 2 yrs.	OAGB		SG		
		53	35(66.0)	56	38(67.8)	0.97 [0.75, 1.27]; (P = 0.84)

a: own calculation (csz-method); * Contacted authors for clarifications.

BPD-DS: Bilio-Pancreatic Diversion with Duodenal Switch; B-SG: Banded Sleeve Gastrectomy; CI: confidence interval; D-RYGB: Distal Roux- en-y Gastric Bypass; HTN: Hypertension; N: number of analysed patients; n: number of patients with (at least one) event; ND: no data; OAGB: One Anastomosis Gastric Bypass;; RCT: randomized controlled trial; RR: relative risk; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve gastrectomy; vs.: versus

Table A18: Results summary for dyslipidemia remission (dichotomous) – RCT, direct comparison: 2 comparisons; 5 studies

Study	Operationalization	Intervention		Comparator		Intervention vs. Comparator
		N	n(%)	N	n(%)	RR [95% -CI]; (p-value)
AGB vs. RYGB (1 study)						
Angrisani 2007 *Class III obesity. 1 person with T2D, 4.15% DL*	Normal blood lipid levels in the absence of hypolipidemic drugs (LDL<100 mg/dl; HDL<440 mg/dl; Triglycerides<150 mg/dl). FU: at 5 yrs.	0	0 (0)	2	1(50)	-
SG vs. RYGB (4 studies)						
Karamanakos 2008 *Class III obesity;16.6% T2D; no information on DL*	Resolution of HDL. FU: at 3 yrs.	3	2(66.7)	4	4(100)	0.69 (0.31, 1.57); (P = 0.38)
	Resolution of LDL. FU: at 3 yrs.	8	6(75)	9	9(100)	0.83 (0.53, 1.31); (P = 0.43)
	Resolution of TG. FU: at 3 yrs.	3	2(66.7)	5	5(100)	0.68 (0.31, 1.51); (P = 0.35)
Peterli 2014-SMBOSS *Class III obesity;*	No symptoms and/or no medication. FU: at	68	29(42.6)	53	33(62.3)	**0.68 (0.48, 0.97)**; (P = 0.03)

24.9% T2D, 59.1% DL	5 yrs.					
Salminen 2018-SLEEVEPASS *Class III obesity; 42.1% T2D, 37.5% DL*	Discontinued DL medications. FU: at 5 yrs.	30	29(96.7)	40	33(81.5)	0.78 (0.49, 1.23); (P = 0.28)
Wallenius 2020-CONTROL *Class III obesity; 100% T2D, 88% DL*	Normal lipid panel without medications. FU: at 2 yrs.	23	9(39.1)	22	12(54.5)	0.72 (0.38, 1.36); (P = 0.31)

a: own calculation (csz-method)

AGB: Adjustable Gastric Banding; CI: confidence interval; DL: Dyslipidemia; dl: deciliter; HDL: High Density Lipoprotein cholesterol; LDL: Low Density Lipoprotein cholesterol; N: number of analysed patients; mg: milligrams; n: number of patients with (at least one) event; ND: no data; RCT: randomized controlled trial; RR: relative risk; vs.: versus; RYGB: Roux -en-Y Gastric Bypass; SG: Sleeve Gastrectomy; TG: Triglycerides

Table A19: Results summary for systolic blood pressure (continuous) – RCT direct comparison: 5 comparisons; 6 studies

Study	Operationalization	Intervention			Comparator			Intervention vs. Comparator
		N	Values at start of study Mean (SD)	Change at end of treatment Mean (SD)	N	Values at start of study Mean (SD)	Change at end of treatment Mean (SD)	MD [95%-CI]; (p-value)
AGB vs. RYGB (1 study)								
Courcoulas 2014 TRIABETES[1]	*SBP (mm Hg)* *2 yrs*	*20*	*128.1 (14.48)*	-7.37 (SE 3.49/SD 15.5)	*18*	*119.98 (12.95)*	-18.7 (SE 3.35/SD 14.2	**11.33**[1.83,20.83] (P =0.02)
	5 yrs	*20*	*134.06(18.66)*	-0.02 (SE 4.29/SD 19.2)	*18*	*116.46 (19.48)*	-1.95 (SE 4.76/SD 20.2)	1.93 [-10.64, 14.50]
BPD-DS vs. RYGB (1 study)								
Aasheim 2009[1]	*2 yrs*	*29*	*121 no SD*	-14.3 (13.67)	*31*	*125 no SD*	-10.8 (13.63)	-3.50 [-10.41,3.41] (P =0.32)
	5 yrs	*29*	*122 no SD*	-16.3 (19.72)	*31*	*126 no SD*	-7.9 (21.54)	-8.40 [-18.84,2.04] (P =0.11)

BPD vs. RYGB (1 study)								
Mingrone 2012 DIBASY[2]	*2 yrs*	*19*	*129.21(8.04)*	-14.55 (12.63)	*19*	*132.11 (10.45)*	-9.02 (7.57)	*% change from BL* -5.53 [-12.14, 1.08]
	5 yrs	*19*	*129.2 (5.8)*	-26.6 (27.6)	*19*	*132.5 (6.2)*	-15.0 (18.6)	-11.10 [-26.07,3.87] (P =0.15)
D-RYGB vs. RYGB (1 study)								
Svanevik 2015[3]	*2 yrs*	*56*	*138 no SD*	-9.3(17.9)	*57*	*131 no SD*	-7.3 (17.0)	-2.00 [-8.44,4.44] (P =0.54)
SG vs RYGB (2 studies)								
Schauer 2014 STAMPEDE[4]	*3 yrs*	*49*	*NR*	-4.43 (20.69)	*48*	*NR*	1.29 (20.38	-5.72 [-13.89, 2.45] (P =0.17)
	5 yrs	*49*	*128.3 (11.6)*	-8.3 (20.4)	*48*	*131.4 (18.79*	-3.3 (22.8)	-5.00 [-13.62, 3.62]
Wallenius 2020 CONTROL[5]	*2 yrs*	*22*	131.3 (16.1)	10.7 (25)	*25*	137.9 (15.9)	-2.1 (18.1)	12.80 [0.17, 25.43] (P =0.05)

AGB: Adjustable Gastric Banding; CI: confidence interval; Hg: MD: mean difference; mm: millimetre; N: number of analysed patients; ND: no data; RCT: randomized controlled trial; SD: standard deviation; SMD: squared mean difference; vs.: versus

1 Courcoulas/TRABETES and Aasheim: No information on the use of antihypertensive drugs; 2 Mingrone/DIBASY: The need for CVD drugs first decreased in both groups, and started to increase again in patients with RYGB after 2 years, while in the BPD group the reduction are stable and close to zero up to last follow-up at 5 years; 3 Svanevik: Sixteen of 20 patients (80%) and 17 of 25 patients (68%) had stopped using antihypertensive medication after RYGB and D-RYGB, respectively (P =. 41); 4 Schauer/STAMPEDE: Mean no of CVD medications decreased from BL to 5 years in both groups (RYGB: from 2.61 to 1.10, and SG: from 2.45 to 1.36), and at 5 years FU 22 patients with RYGB and 12 patients with SG had not diabetes medication; 5 No of patients without HTN

Table A20: Results summary for diastolic blood pressure (continuous) – RCT direct comparison: 4 comparisons; 6 studies

Author year	**FU**	**Intervention**			**Comparator**			**Intervention vs. Comparator**
		N	**Values at start of study Mean (SD)**	**Change at end of treatment Mean (SD)**	**N**	**Values at start of study Mean(SD)**	**Change at end of treatment Mean (SD)**	**MD [95%-CI]; (p-value)**
AGB vs. RYGB (1 study)								
Courcoulas 2014 TRIABETES[1]	*2 yrs*	*20*	*75.17 (8.91)*	-1.75 (2.06)	*18*	*71.06 (7.66)*	-8.41 (2.07)	**6.66** [5.34,7.98] (P <0.00001)
	5 yrs	*20*	*79.53 (8.59)*	1.54 (2.21) 8	*18*	*72.16 (9)*	-6.92 (2.42)	8.46 [6.98, 9.94]
BPD-DS vs. RYGB (2 studies)								
Aasheim 2009[1]	*2 yrs*	*29*	*77.4 no SD*	-10.7 (11.3)	*31*	*76.8 no SD*	-5.46 (11.12)	-5.24 [-10.92,0.44]

								(P =0.07)
	5 yrs	*29*	*77no SD*	-11.1 (14.19)	*31*	*78 no SD*	-4.8 (14.17)	6.30 [-0.88;13.48] (P =0.09)
BPD vs. RYGB (1 study)								
Mingrone 2012 DIBASY[2]	*2 yrs*	*19*	*82.37 (4.21)*	-13.06 (8.97)	*19*	*84.21 (4.79)*	-7.3 (9.42)	*% change from BL:* -5.76 [-11.61, 0.09]
	5 yrs	*19*	*83.5 (3)*	-12.4 (11.9)	*19*	*84.2 (3.5)*	-8.3 (13.5)	4.10 [-3.99,12.19] (P =0.32)
D-RYGB vs. RYGB (1 study)								
Svanevik 2015[3]	*2 yrs*	*56*	*80 no SD*	-1.2 (11.6)	*57*	*78 no SD*	-2.4 (11.9)	1.20 [-3.13, 5.53] (P =0.59)
SG vs RYGB (2 studies)								
Schauer 2014 STAMPEDE[4]	*3 yrs*	*49*	*NR*	-6.27 (13.3)	*48*	NR	-4.25 (10.57)	-2.02 [-6.80, 2.76] (P =0.41)
	5 yrs	*49*	*84.11 (11.45)*	-8.1 (14.7)	*48*	*75.98 (11.57)*	-5.8 (12.5)	-2.30 [-7.77,3.17]
Wallenius 2020 CONTROL[5]	*2 yrs*	*22*	83.2 (12.5)	2.6 (14.4)	*25*	86.8 (8.4)	-7.5 (8.3)	10.10[3.26,16.94] (P =0.004)

CI: confidence interval; Hg: mercury MD: mean difference;mm: millimetre; N: number of analysed patients; ND: no data; RCT: randomized controlled trial; SD: standard deviation; SMD: squared mean difference; vs.: versus								

1 Courcoulas/TRABETES; Aasheim: No information on the use of antihypertensive drugs; 2 Mingrone/DIBASY: The need for CVD drugs first decreased in both groups, and started to increase again in patients with RYGB after 2 years, while in the BPD group the reduction are stable and close to zero up to last follow-up at 5 years; 3 Svanevik: Sixteen of 20 patients (80%) and 17 of 25 patients (68%) had stopped using antihypertensive medication after RYGB and D-RYGB, respectively (P =. 41); 4 Schauer/STAMPEDE: Mean no of CVD medications decreased from BL to 5 years in both groups (RYGB: from 2.61 to 1.10, and SG: from 2.45 to 1.36), and at 5 years FU 22 patients with RYGB and 12 patients with SG had no diabetes medication; 5 No of patients without HTN

Table A21: Mean difference in change from BL for total cholesterol, HDL, LDL, and triglycerides at 2, 3 and 5 years follow-up*; 6 comparisons; 8 studies

Author Year		**Arms**	**No of pts.**	**Total cholesterol (mmol/L)**	**HDL (mmol/L)**	**LDL (mmol/L)**	**Triglycerides (mmol/L)**
AGB vs RYGB (1 study)							
Courcoulas 2015 TRIABETES		AGB	17	-0.27 (SE 0.25)	0.21 (0.06)	0.10 (0.23)	-0.74 (0.21)
		RYGB	18	-0.17 (SE 0.24)	0.40 (0.06)	0.13 (0.22)	- 0.93 (0.19)
	MD in change from BL -2 yrs FU			-0.10 (-,0.78, 0.58)	**-0.19 (-0.36,-0.02,)**	-0.03 (-0.65, 0.59)	0.19 [-0.37,0.75]

Courcoulas 2015 TRIABETES		AGB	20,21, 21,21	0.064 (0.22)	0.285 (0.061)	0.17 (0.21)	-0.551 (0.194)
		RYGB	16,20, 20, 20 check	-0.34 (0.22)	0.43 (0.061)	-0.013 (0.20)	-1.076 (0.193)
	MD in change from - BL 3 yrs FU			Not included	Not included	Not included	Not included
Courcoulas 2020 TRIABETES		AGB	20, 21, 21,21	-0.182 (SEM 0.183)	*0.289 (0.066)*	*-0.197 (0.246)*	*-0.499 (0.34)*
		RYGB	16, 20, 20, 20	-0.29 (SEM 0.20)	*0.458 (0.071)*	*-0.244 (0.214)*	*-0.88 (0.355)*
	MD in change from BL- 5 yrs FU			0.11 [-0.42,0.64]	-0.17 [-0.36, 0.02]	0.05 [-0.59, 0.69]	0.38 [-0.58, 1.34]
SG vs RYGB (3 studies)							
Peterli 2018		SG	68	0.63 (0.23 to 1.034)	0.44 (0.36 to 0.53)	0.26 (-0.018 to 0.54)	0.9 (0.677 to 1.13)

SMBOSS							
		RYGB	53	0.44 (0.15 to 0.737)	0.55 (0.455 to 0.647)	0.59 (0.36 to 0.82)	0.87 (0.577to 1.16)
	MD in change from BL-5 yrs			0.19 [-0.29, 0.67]	-0.11 [-0.23, 0.01]	-0.33 [-0.69, 0.03]	0.03 [-0.33, 0.39]
Schauer 2014[3] STAMPEDE		SG	49	NR	35.0 (31.0)	14.5 (62.2)	-31.5 (-52.1 to -6.9)
		RYGB	48	NR	% change from BL 37.7 (27.3)	% change from BL 16.9 (54.4)	Median% change from BL -45.9(-61.0 to -7.5)
	MD in % change from BL-3 yrs			NA	NS	NS	NS
Schauer 2017 STAMPEDE		SG	47	NR	29.5 (29.5)	16.6 (48.6)	-29.4 (-51.4 to -2.9)
		RYGB	48	NR	*% change from BL:* 31.9 (29.1)	*% change from BL:* 12.4 (53.8)	*% **median** change from BL*: -39.8 (-58.4 to 74)
	MD%in change			NA	-2.30 [-14.09, 9.49]	4.20 [-16.62,25.02]	No difference between

	from BL-5 yrs						groups.
Wallenius 2020		SG	22	0.05 (1.02)	0.37(0.26)	0.05 (0.88)	-1.52 (1.88)
		RYGB	25	-0.02 (1.11)	0.43 (0.33)	-0.02 (1.00)	-1.15 (1.12)
	MD in change from BL-2 yrs			0.07(-0.54, 0.68)	-0.06 (-0.23, 0.11)	0.07 (-0.47. 0.61)	-0.37 (-1.27, 0.53)
D-RYGB vs. RYGB (1 study)							
Risstad 2016 (Svanevik 2015)		D-RYGB	56	-1.24 (-1.45; -1.03)	0.31(0.26;0.36)	-1.24(-1.40; -1.06)	-0.71(-0.84: -0.58)
		RYGB	57	-0.49 (-0.70; -0.28)	0.52 (0.44;0.57)	-0.73 (-0.88; -0.54)	-0.60(-0.73; -0.47)
	MD in change from BL-2 yrs			**-0.75 (-1.04,-0.46**)	**-0.21 (-0.30,-0.12)**	**-0.51 (-0.72,-0.30)**	-0.11 [-0.29, 0.07]
OAGB vs RYGB (1 study)							
Robert 2019[1] YOMEGA		OAGB	56, 55, 53,86	-0.4(1.1)	0.3 (0.3)	-0.4 (1.1),	-0.6 (1.5),

Questionable data that needs clarifying. No response from authors.		RYGB	49, 50, 49, 91	-0.3 (1.0)	0.3(0.3)	-0.4 (1.1)	-0.7 (0.61)
	MD in change from BL at 2 yrs			-0.10 (-0.50, 0.30)	0.00 (-0.11,0.11)	0.00 (-0.41, 0.41)	0.10 [-0.14, 0.34]
BPD-DS vs RYGB (1 study)							
Aasheim 2009; Søvik 2011; Risstad 2015		BPD-DS	29	-1.07 (-1.35; -0.79)	0.12 (0.04;0.20)	-0.76 (-0.96; -0.61)	-0.80 (-1.00;- 0.60)
		RYGB	31	-0.24 (-0.50: 0.03)	0.37 (0.29; 0.45)	-0.26 (-0.43; -0.09)	-0.83 (-1.02; -0.63)
	MD in change from BL -2 ys FU			**-0.83 (-1.20,-0.46)**	**-0.25(-0.36,-0.14)**	**-0.50 (-0.75,-0.25)**	0.03 [-0.23, 0.29]
Aasheim 2009; Søvik 2011, Risstad 2015		BPD-DS	29	-1.19 (-1.47 to -0.931)	0.336 (0.207 to 0.44)	-0.983 (-1,24 to -0.72)	-1.2 (-1.43 to -0.95)
		RYGB	31	0.078 (-0.18 to 0.362)	0.569(0.465 to 0.698)	-0.13(-0.36 to 0.13)	-0.756 (-0.99 to -0.52)

	MD in change from BL -5 yrs FU			-1.27 [-28.06, 25.52]	**-0.23 [-0.39, -0.07]**	**-0.85 [-1.18, -0.52]**	**-0.44 [-0.76. -0.13]**
BPD vs. RYGB (1 study)							
Mingrone 2012-DIBASY		BPD-DS	19,19,19,19	-49.25 (11.52)	12.98 (20.66)	-64,63 (15.93)	-56.79 (16.70)
		RYGB	19,10,19,19	*% change from BL:* -6.83 (27.03)	*% change from BL:* 29.66 (18.21)	*% change from BL:* -17.21 (36.21)	*% change from BL:* -21.17 (41.23)
	MD in change from BL- 2 yrs			**-42.42 [-55.63.-29.21]**	**-16.68 [-31.27-2.09]**	**-47.42 [-65.21,-29.63,]**	**-35.62 [-55.62, -15.62,]**
Mingrone 2015		BPD-DS	19	-2.6(1.4)	0.14 (0.19)	-2.2 (1.1)	-1.2 (0.9)
		RYGB	19	-0.3 (1.3)	0.28 (0.17)	-0.4 (1.2)	-0.4 (0.8)
	MD in change from			**-2.30 [-3.16,-1.44]**	**-0.14 [-0.25,-0.03]**	**-1.80 [-2.41,-1.19,]**	**-0.80 [-1.34,-0.26]**

	BL -5 yrs						

*Mean change from BL if not otherwise stated.

1 Probably incorrect data. Contacted authors but no response. Large losses to follow-up! 91 RYGB and 86 OAGB had 2 yrs FU- but not all of these patients provided data on lipids.2 Salminen 2018 do not report MD in change from BL, only MD between groups at different time points.3 Shauer 2014-2015? Reports Mean Difference% change from BL (or median% difference). No differences between procedures.

Table A22: Summary of results of health related quality of life (HRQOL) across studies and comparisons: 6 comparisons; 11 studies

Author Year	Procedure	FU	No part.	QOL instrument	Mean score	SD	95%CI	Mean change from BL	SD	95% CI	Comment
SG vs RYGB (5 studies)											
Ignat 2017	SG	BL	29	M-A-QoLQII	0.3	1.0	-	NR	-	-	No differences between groups.
	RYGB		37		0.5	0.9	-	NR	-	-	
	SG	2 yrs	29		1.5	0.7	-	NR	-	-	
	RYGB		37		1.7	0.6	-	NR	-	-	
	SG	3 yrs			1.5	0.7	-	NR	-	-	
	RYGB				2.1	0.5	-	NR	-	-	
	SG	5 yrs			1.4	1.0	-	NR	-	-	

	RYGB				1.2	1.1	-	NR	-	-	
	SG	BL		GIQLI[8]	90·7	16.3	-	NR	-	-	No differences between groups.
	RYGB				96·4	16.0	-	NR	-	-	
	SG	2 yrs			114.5	17.6	-	NR	-	-	
	RYGB				113.3	15.6	-	NR	-	-	
	SG	3yrs			113.1	11.5	-	NR	-	-	
	RYGB				113.4	15.6	-	NR	-	-	
	SG	5 yrs			113.0	16.6	-	NR	-	-	
	RYGB				111.7	17.8	-	NR	-	-	
Peterli 2014-SMBOSS	SG	BL	101	GIQLI	99.7		95.6 to 103.8				No differences between groups.
	RYGB		104		99.3		95.9 to 102.7				
	SG	5 yrs			113.6		108.9 to 118.3	18.9		13.7 to 24.1	
	RYGB				117.9		114.8 to 121.0	18.1		14.7 to 21.5	
	SG	BL		BAROS	0.1		−0.1 to 0.3				
	RYGB				0.2		−0.1 to 0.5				
	SG	5 yrs			1.4		1.1 to 1.7	1.3		1.0 to 1.6	
	RYGB				1.7		1.5 to 1.9	1.4		1.1 to 1.7	

Salminen 2018-SLEEVEPASS	SG	5 yrs	95	M-A-QoLQII	0.10	0.94	-	-	-	-	No differences between groups.
	RYGB		98		0.12	1.12	-	-	-	-	
	SG	5 yrs			0.85	1.08	-	-	-	-	
	RYGB				0.76	1.01	-	-	-	-	
Schauer 2017-STAMPEDE	SG	5 yrs	50	RAND-36[9]	Total scores NR		-	-	-	-	No differences between groups.
	RYGB		50				-	-	-	-	
Zhang 2014	SG	5 yrs	26	M-A-QoLQII	1.33	0.8	-	-	-	-	No differences between groups
	RYGB		28		1.58	0.71	-	-	-	-	
D-RYGB vs RYGB (1 study)											
Svanevik 2015	D-RYGB	BL	56	SF-36-MCS[4]	48.0		45.3 to 50.8				No differences between groups
	RYGB		57		49.2		46.5 to 51.9				
	D-RYGB	2 yrs			49.6		46.9 to 52.3	1.6		-1.4 to 4.5	
	RYGB				50.8		48.1 to 53.5	1.6		-1.4 to 4.6	
	D-RYGB	BL	56	SF-36-PCS[4]	36.1		33.7 to 38.5				
	RYGB		57		38.0		35.6 to 40.4				
	D-RYGB	2 yrs			50.2		47.8 to 52.6	14.1		11.8 to 16.4	
	RYGB				49.0		46.6 to 51.4	11.0		8.6 to 13.3	

	D-RYGB	BL		M-A-QoLQII[5]	0.24		0.00, 0.48				
	RYGB				0.47		0.24, 0.71				
	D-RYGB	2 yrs			0.99		0.71 to 1.28	0.75		0.49 to 1.01	
	RYGB				1.14		0.85 to 1.43	0.67		0.38 to 0.95	
	D-RYGB	BL		OWLQOL[6]	35.2		29.9, 40.5				
	RYGB				37.7		32.4, 42.9				
	D-RYGB	2 yrs			74.3		69.5, 79.2	39.1		32.9, 45.3	
	RYGB				77.4		72.6, 82.2	39.8		34.9, 44.7	
OAGB vs RYGB (1 study)											
Robert 2019-YOMEGA	OAGB	2 yrs		QOL-IWQOL[7] and BAROS	Total scores NR		-	-	-	-	No differences between groups
	RYGB						-	-	-	-	
BPD-DS vs RYGB (1 study)											
Aasheim 2009	BPD-DS	2 yrs	28	SF-36[1]	Total scores NR	-	-	-	-	-	Greater SF-36 score for RYGB in one of eight sub-scores.
	RYGB		30								
	BPD-DS	5 yrs									No differences between groups
	RYGB										

	BPD-DS	2 yrs	29	Obesity related problem scale[2] (psychosocial functioning)				-27.7		-37.1 to -18.3	
	RYGB		31					-32.5		-42.2 to -22.8	
	BPD-DS	5 yrs			35.2%		26.4 to 44.0				
	RYGB				24.3%		15.5 to 33.2				
BPD vs. RYGB (1 study)											
Mingrone 2012 DIBASY	BPD	5 yrs	19	SF-36	77.5	19.0	-	-	-	-	Greater SF-36 score for RYGB in three of 10 areas.
	RYGB		19		85.6	17.4	-	-	-	-	
B-SG vs. SG (1 study)											
Fink 2020-MISO	B-SG	3 yrs	46	BAROS[3]	6.44	NR	-	NR	-	-	Higher QOL score in BSG group.
	SG		44		4.98	NR	-	NR	-	-	
B-RYGB vs RYGB (1 study)											
Rasera 2018	SR-RYGB		138	BAROS	Total scores NR.						No differences between groups
	RYGB		147								

[1] SF-36, 36-Item Health Survey that range from 0 to 100, with higher scores indicating better health. [2] Obesity related problem scale: a self-assessment module developed to measure the impacts of obesity on psychosocial functioning [3]BAROS: the Bariatric Analysis and Reporting Outcome System. [4] SF-36 MCS and PCS: SF-36 Norm-Adjusted Dimensional Scores and Summary Scores [5]The Moorehead–Ardelt Quality of Life Questionnaire II (M-A-QoLQII). Six areas are examined: self-esteem, physical well-being, social relationships, work, sexuality and eating behaviour. Each item is evaluated on a 10-point scale and scored from −0·5 to +0·5. [6]OWLQOL Obesity and Weight-Loss Quality of Life Scores. [7] IWQOL: Impact of weight on quality of life. [8]The Gastrointestinal Quality of Life Index (GIQLI) is a health-related QoL questionnaire for gastrointestinal diseases. It explores the patient's self-evaluation of the 2-week interval before completion of the questionnaire. It includes 36 items covering four domains: gastrointestinal symptoms (19 questions), physical function (7 questions), social function (4 questions), emotional function (5 questions), and one item about subjective treatment assessment. Each item is scored from 0 (least desirable option) to 4 (most desirable option). The GIQLI score is obtained by summing each item, and theoretically ranges from 0 to 144.[9] Same as the SF-36.

Table A23: Length of hospital stay (LOS): initial procedure, readmission, and ICU stay (or people requiring ICU care): 8 comparisons; 11 studies

Author Year	Procedure	Hospital LoS, nean ±SD if not otherwise stated			
		Initial procedure	Early readmissions (<30d)	Late readmissions (>30d)	ICU
AGB vs RYGB (2 studies)					
Angrisani 2007	AGB	2 ± 1 d	-	2-7 d (6 pts.)	-
	RYGB	4 ± 2 d	3 d (1 pts.), 6 mo (2pts.)	3-11 d (6 pts.)	40 d (1 pts)
Nguyen 2009	AGB	1.5 ± 1.1 d	-		1 person
	RYGB	3.1 ± 1.5 d	-		3 people
SG vs RYGB (4 studies)					
Hofsø 2019 -OSEBERG	SG	Median: 1 d (range 1–6)	-		-
	RYGB	Median:1 d (range 1–4)	-		-
Ignat 2017	SG	-	Mean: 0.3 d (10/55)		-

	RYGB	-	Mean: 2.3 d (25/45)		-
Paluszkiewicz 2012	SG	Median: 6.0 d (4-77)	-		-
	RYGB	Median: 6.0 d (4-9)	-		-
Wallenius 2020 CONTROL	SG	3.0 ± 1.4	-		-
	RYGB	2.5 ± 6.8	-		-
D-RYGB vs RYGB (1 study)					
Svanevik 2015	D-RYGB	Median: 2 d (1–24)	-		-
	RYGB	Median: 2 d (1–4)	-		-
OAGB vs RYGB (1 study)					
Robert 2019-YOMEGA	OAGB	Median: 5 d (4-5)	-		-
	RYGB	Median: 5 d (4-6)	-		-
OAGB vs SG (1 study)					
Seetharamaiah 2017	OAGB	3.20 ± 0.64 d	-		-
	SG	3.95 ± 0.73 d	-		-
BPD-DS vs RYGB (1 study)					
Hedberg 2012	BPD-DS	7.6 ± 5.4	-		-
	RYGB	5.5 ± l.2	-		-

B-SG vs SG (1 study)					
Tognoni 2016	B-SG	-	7 d (one person)		-
	SG	-	5 d (one person)		-
B-RYGB vs RYGB (1 study)					
Arceo-Olaiz 2008	SR-RYGB	6 ± 6 d	-		-
	RYGB	7 ± 6 d	-		-

Table A24: All adverse events reported in the included studies including their classifications (N=28)

Author Year	Procedure	Classification	AEs	Classification
Angrisani 2007; Angrisani 2013	RYGB	Early	Posterior pouch **leak** (1), Jejunal **perforation** (1);	*Major/minor AEs not distinguished*
	AGB	Early	-	
	RYGB	Late	**Internal hernia** (1), Gallstones (4), **Incisional hernia** on trocar site (1)	
	AGB	Late	**Band removal** due to gastric pouch dilation (4), band erosion (1), untreatable reflux symptoms (1). **Conversion** due to inefficiency (4).	
Arceo-Olaiz 2007; Zarate 2013	RYGB		Gastric **Leak** not requiring reoperation (1), **internal hernia** (1), Vomiting (4)	*AEs not categorised by time or severity.*
	SR-RYGB		Gastric **Leak** not requiring reoperation (1), gastric outlet **obstruction** (1), **internal hernia** (1), Vomiting (5)	
	Unspecified group		Trocar port hernia (1)	
Aasheim/Søvik 2010; 2011	RYGB	Early	Intra-abdominal **abscess** (1), cutaneous abscess (1), acute abdominal pain (2), anastomotic **leak** (2), intraluminal **hemorrhage** (1), subcutaneous	*AEs not categorised by severity.*

			hemorrhage (1), pneumonia (1), hyperglycemia (1). Two re-operations required.	
	DS	Early	Intra-abdominal **abscess** (2), cutaneous abscess (1), **leak** from duodenal stump (2), intraluminal **hemorrhage** (1), **stenosis** of duodeno-ileostomy (1), pneumonia (1), infection of unknown origin (1), dyspnea and chest pain (1), gluteal musculature ischemia (1). One re-operation required.	
	RYGB	Late	Vomiting (1), abdominal pain (4), diarrhea (1), small-bowel **obstruction** (1), cholelithiasis (3) psychiatric disorder (1), severe depression (1)	
	DS	Late	Vomiting (3), abdominal pain (1), diarrhea (1), inflammation of transverse mesocolon (1), common bile duct stones (1), intra-abdominal **abscess** (1), pneumonia (1), severe edema of lower extremities (1), peritonitis (1), iron deficiency (1), small-bowel **obstruction** (1), cholelithiasis (2), protein-calorie malnutrition (3), night blindness (2), hepatic failure (1), urolithiasis (1), traumatic subarachnoid hemorrhage (1), traumatic fracture of the humerus (1)	
Aasheim 2009/Risstad 2015[1]	RYGB	Late (Gastrointestinal)	Cholelithiasis (3), **internal hernia** (2), peptic ulcer (1), gastrointestinal **bleeding** (1), pouchitis (1), anorectal disease (1), diverticulitis (1), appendicitis (1), enterocolitis (1)	*Study categorised AEs not by severity but by type*
	DS		Cholelithiasis (7), elongation of common channel (3), **internal hernia** (1), bowel **obstruction** (1), inflammation of transverse mesocolon (1), peritonitis (1), liver failure (1), peptic ulcer (1), gastrointestinal **bleeding** (1), anorectal disease (3), intraabdominal abscess (1)	
	RYGB	Late (gastrointestinal symptoms)	Nausea/vomiting (4), acute abdominal pain (3), chronic abdominal pain (2), diarrhea (1)	
	DS		Nausea/vomiting (4), acute abdominal pain (1), diarrhea (1)	
	RYGB	Nutritional	**Iron deficiency requiring blood transfusion** (1)	
	DS		Night blindness due to vitamin A deficiency (2), **protein-caloric malnutrition requiring hospitalisation** (4), **iron deficiency requiring blood transfusion** (5)	
	RYGB	Infections	UTI (1), hidradenitis (1), erysipelas (2)	

	DS		Pneumonia (2), UTI (1), hidradenitis (1), severe pilonidal disease (1), scrotal abscess (1)	
	RYGB	Other	Miscarriage/stillbirth (2), severe psychiatric illness (2), type 1 diabetes mellitus (1), cancer (2), noncardiac chest pain (1), thromboembolic disease (1),	
	DS		Urethral stone (4), hypoglycemia (1), traumatic fracture (2), **osteoporosis** (1), traumatic subarachnoid bleeding and meningitis (1), severe psychiatric illness (2), alcohol abuse (1), noncardiac chest pain (1), cardiomyopathy (1), serious nose bleeding (1), headache (1)	
Capristo 2018	RYGB		Hypoglycemia requiring admission to hospital (4), Dehydration requiring admission to hospital (4), Cholelithiasis (2), Nutritional deficiencies (18)	*Major/minor and Early/late AEs not distinguished*
	SG		Dehydration requiring admission to hospital (3), Nutritional deficiencies (11)	
Courcoulas 2014[2]	RYGB	Major	**Anastomotic Ulcer** (1; 5%)	*Early/late AEs not distinguished*
	LAGB		**Dehydration requiring hospital admission** (2; 9.5%)	
	RYGB	Other	Prolonged LOS: elevated blood glucose, pain, nausea (3; 15%), nausea and emesis **requiring IV hydration** (1; 5%)	
	LAGB		Prolonged LOS: elevated blood glucose, pain, nausea (3; 14.3%), **port malposition requiring operation** (1; 4.8%), pruritis/erythema at incision site (1; 4.8%), abdominal pain (1; 4.8%)	
Courcoulas 2015	RYGB	Early, major	-	
	LAGB		-	
	RYGB	Late, major	**Anastomotic ulcer** (1)	
	LAGB		**Overfilled gastric band** (2), Vertigo and hypertension (1)	
	RYGB	Early, minor	Prolonged hospital stay (2), nausea and emesis **requiring IV drip** (1)	
	LAGB		Prolonged hospital stay (4), Pruritis erythema at incision site (1), Abdominal pain (1)	
	RYGB	Late, minor	-	
	LAGB		**Port malposition** (1)	
	RYGB	Other	Renal lethiasis (1)	
	LAGB		Hypotension and lightheadedness (1), Dehydration (2)	

Courcoulas 2020	RYGB	Early	**Prolonged postoperative stay** (2)	*AEs not categorised by severity.*
	AGB		**Prolonged postoperative stay** (4), Incisional pain (1), abdominal pain (1)	
	RYGB	Late	Stent (1), respiratory pneumonia (1), **nutritional and metabolic dehydration** (1), **anemia requiring transfusion** (1), neurologic urology (2), stone (1), plastic surgery (1), orthopedic surgery (1), orthopedic fracture (2), **bariatric reoperation** (1), **anastomotic ulcer** (1), appendectomy (1), cholecystectomy (1), hysterectomy (1), upper endoscopy (1).Note: *Unclear if the bariatric reoperations were due to inefficiency.*	
	AGB		Cardiovascular vertigo and hypertension resulting in **hospital admission** (1), hypotension and lightheadedness (1), **nutritional and metabolic dehydration** (2), stent (1), stone (1), plastic surgery (3), orthopedic surgery (6), **bariatric reoperation (1**), **port malposition** (1), **overfilled gastric band resulting in hospital admission** (2), diabetes related eye complications (1), skin cancer (2)	
Fahmy Moustafa 2018	RYGB	Early	**Hemorrhage** (3; 10%), dumping (1; 3.3%), diarrhea (2; 6.7%), **stricture** (1; 3.3%), anemia (4; 13.3%), **port site hernia** (1; 3.3%), Hyperemia - erosions ± ulcerations (2; 6.7%), hyperemic gastritis (17; 56.7%), no gastritis (11, 36.7%), esophagitis (7, 23.3%)	*AEs not categorised by severity.*
	OAGB		**Hemorrhage** (2; 6.7%), dumping (3; 10%), diarrhea (1; 3.3%), anemia (3; 10%), Hyperemia - erosions ± ulcerations (7, 23.3%), hyperemic gastritis (16, 53.3%), no gastritis (7; 23.3%), esophagitis (17; 56.7%)	
Fink 2020/MISO	RYGB	Late, major	Ring slippage (1; 2.2%), GERD with conversion to RYGB (2, 4.4%)	*Major early AEs was not included in the study*
	SG		GERD with conversion to RYGB (1; 2.2%), incisional hernia (1; 2.2%)	
	RYGB	Early, minor	-	
	SG		Bleeding (1; 2.1%)	
	RYGB	Late, minor	Regurgitation ≥1/wk (6; 13.3%), gastroesophageal reflux RSI >13 (3; 6.5%), symptomatic cholelithiasis (2; 4.4%)	
	SG		Regurgitation ≥1/wk (2; 4.3%), gastroesophageal reflux RSI >13 (4; 8.7%),	

			sleeve stenosis (1; 2.2%), symptomatic cholelithiasis (2; 4.3%)	
Hedberg 2012	RYGB	Early	**reoperation (1)**	
	BPD-DS		**reoperation** (2)	
	RYGB	Late	Readmission for unclear abdominal pain (1), incisional hernia (2)	
	BPD-DS		Readmission because of cholecystitis (1), incisional hernia (3)	
Himpens 2006	GB	Early	-	*AEs not categorised by severity.*
	SG		**Intraperitoneal bleeding** (1), **gastric ischemia** (1)	
	GB	Late	Band related problems: Pouch dilation (3), gastric erosion (1), disconnection (3), inefficiency (2)	
	SG		Inefficiency (2)	
Hofsø 2019/OSEBERG	SG	Early, Severe	**Postoperative bleeding** (1)	*Early AEs were separated into mild, moderate, severe and death. (no deaths were recorded) Late AEs were separated by medical and surgical conditions*
	RYGB		**Anastomotic ulcer** (1)	
	SG	Early, Moderate	Dysphagia (1)	
	RYGB		Clostridium difficile colitis (1)	
	SG	Early, Mild	Campylobacter jejuni enteritis (1), abdominal pain (3), hypotension (1), umbilical hernia (1)	
	RYGB		Pulmonary infiltration (1), urolithiasis (1), abdominal pain (2), transient renal insufficiency (1), fever (1), hypotension (1), diarrhea (1)	
	SG	Late	**Acute myocardial infarction** (1), chest pain (2), neuropathic pain in feet (1), hematochezia (1), UTI (1), depression (1), cholelithiasis (1), appendicitis (1), fecaloma (1), urolithiasis (1), cervical intraepithelial neoplasia (1), abdominal pain (4), minor traumatic musculoskeletal injuries (3), minor non-traumatic musculoskeletal injuries (3)	
	RYGB		Palpitations (1), bilateral peroneal nerve palsy (1), diarrhea (1), transient thyroiditis (1), skin infection (1), tonsillitis (1), UTI (3), infected benign ovarian tumor (1), respiratory tract infection (2), otitis externa (1), cholelithiasis (1), appendicitis (1), metrorrhagia (1), minor traumatic musculoskeletal injuries (1)	
Ignat 2017	RYGB	Early	anastomotic **bleeding** (1)	*AEs not categorised by major/minor*
	SG		-	

	RYGB	Late	**Anemia** (7), Gastric **perforation** (1), Bowel anastomosis **perforatio**n (1), **Internal hernia** (1), Vomiting (1), Abdominal pain (5), Peptic ulceration (2), Other (3)	
	SG		**GERD** (2), Persistent vomiting (3), Abdominal pain (3)	
Karamanakos 2008; Kehagias2011	RYGB	Early, Major	Intestinal **obstruction** (1), **ventral hernia** (1): **fistula** (1)	
	SG		Leakage in the anastomotic junction (1)	
	RYGB	Late, Major	**Obstructed** ileus (1)	
	SG		Abdominal **abscess** (1)	
	RYGB	Early, Minor	-	
	SG		Acid regurgitation, heartburn, vomiting (20% of patients) up to 6 months	
	RYGB	Late, Minor	-	
	SG		-	
Keidar 2013	RYGB		Vomiting (12); no *deaths recorded*	
	SG		Vomiting (10); *no deaths recorded*	
Mingrone 2012, 2015/DIBASY	RYGB		**Intestinal occlusion** (1; 5%), iron deficiency anemia (3; 16%), **osteopenia** (1; 5%), renal calculus (1; 5%), nephropathy (1; 5%), symptomatic hypoglycemia (2; 11%)	*No late AEs occurred*
	BPD		**Incisional hernia (**1; 5%), iron deficiency anemia (5; 26%), hypalbuminaemia (3; 16%), **osteopenia** (3; 16%), **osteoporosis** (1; 5%), transient nyctalopia (1; 5), renal calculus (2; 11%)	
Murphy 2018	RYGB		**Stricture** (4; 7%), ulcer (3; 5%), anastomotic **leak** (1; 2%), intraabdominal **bleeding** (1; 2%), upper gastrointestinal **bleed** (1; 2%), wound infection (1; 2%), arrythmia or palpitations (1; 2%), renal impairment (1; 2%), **stroke** (1; 2%)	*Major/minor and Early/late AEs not distinguished*
	SG		**Stricture** (4; 7%), upper gastrointestinal **bleed** (1; 2%), wound infection (1;2%), arrythmia or palpitations (1;2%)	
Nguyen 2009[3]	RYGB	Early, Major	Gastrointestinal **hemorrhage** (2), gastrointestinal **obstruction** (4), **internal hernia** (1)	
	AGB		Renal insufficiency (1), gastrointestinal **obstruction** (1)	
	RYGB	Early, Minor	**Dehydration requiring readmission** (4), UTI (2), wound infection (7),	

			prolonged diarrhea (1), clostridium difficile infection (1), ileus (1), gastrointestinal hemorrhage (1)	
	AGB		**Dehydration requiring readmission** (1), UTI (1), clinically significant atelectasis (1), clostridium difficile infection (1)	
	RYGB	Late, Major	Anastomotic **stricture** (17), **internal hernia** (2), ventral hernia (3), death related to alcohol/drug abuse (1), **marginal ulcer requiring revision of anastomosis** (2), abdominal pain requiring laparoscopy (2), bowel **obstruction** (1), peripheral neuropathy (1)	
	AGB		**Port revision** (3), **band erosion/slippage/obstruction** (5), **failure of weight loss requiring revisional surgery** (2)	
	RYGB	Late, Minor	Marginal ulcer (9), gastrointestinal bleeding (2), **severe iron deficiency requiring iron infusion** (3), alcohol/drug abuse (1)	
	AGB		-	
Nguyen 2018	RYGB	Late	**Ventral hernia** (2), **marginal ulcer requiring revision** of anastomosis (1), bowel obstruction (1), peripheral neuropathy (1), marginal ulcer requiring medical management (15), **severe iron deficiency requiring iron infusion** (4), alcohol/drug abuse (4), cancer (1), cholecystitis (11), death (2)	*Only late AEs reported, no distinction between major/minor*
	AGB		**Port revision** (3), **band erosion/slippage/obstruction** (17), alcohol/drug abuse (1), kidney stones (1), **poor weight loss requiring revisional surgery (**5), cancer (1), cholecystitis (4)	
Paluszkiewicz 2012	RYGB	Early	Infection (2), fluid collection (4)	*No distinction between major/minor AEs*
	SG		**Leak** (1), **bleeding** (2), **venous thrombosis** (1), infection (1), fluid collection (2)	
	RYGB	Late	**Incisional hernia** (1), cholelithiasis (1), **serum iron deficiency (9), vitamin B12 deficiency (11)**	
	SG		Cholelithiasis (5), **serum iron deficiency (12), vitamin B12 deficiency (5)**	
Peterli 2014/SMBOSS	RYGB	Early, Major	**Leak** (1), **bleeding** (2), **obstruction** (1), infection (7), death (1)	*Late major/minor not distinguished*
	SG		**Obstruction** (1), infection (1)	
	RYGB	Early, Minor	Dysphagia (2), unspecified surgical AEs (1), unspecified nonsurgical AEs (5)	

	SG		Dysphagia (3), unspecified surgical AEs (1), unspecified nonsurgical AEs (3)	
	RYGB	Late	Small bowel **obstruction** (2**), internal hernia** (9), incisional hernia (1), Gastroscopy necessary: laparoscopy (1), severe dumping (3), **Insufficient weight loss** (2), death (2)	
	SG		**Conversion RYGB due to GERD** (9), incisional hernia (1), **Insufficient weight loss** (5)	
Rasera 2016	RYGB		Death (1), clinical intestinal **obstruction** symptoms treated with balloon dilation (2), **anastomotic ulcers** (2), abdominal wall complications (8.3%)	*No distinction between early/late, major/minor*
	SR-RYGB		Death (1), clinical intestinal **obstruction** symptoms (5) of which 2 treated with balloon dilation, **anastomotic ulcers** (6), abdominal wall complications (8.3%)	
Robert 2019/YOMEGA	RYGB		Anastomotic ulcer (3; 13%), bowel **obstruction** (3; 13%), abdominal pain (5; 21%), vesicular lithiasis (5; 21%), early peritonitis (1; 4%), abdominal wall hematoma or abscess (3; 13%), vomiting (2; 8%), hemo-peritoneum (1; 4%), **gastrogastric fistula** (1; 4%)	*No distinction between early/late, major/minor but is defined as* "Serious adverse events associated with surgery"
	OAGB		**Nutritional complications** (9; 21%), anastomotic ulcer (2; 5%), **GERD (**3; 7%), bowel **obstruction** (1; 2%), diarrhea or anal fissures (6; 14%), vesicular lithiasis (8; 19%), urinary lithiasis (3; 7%), early peritonitis (3; 7%), incisional hernia (1; 2%), kidney failure by dehydration (1; 2%), anticoagulant overdose (1; 2%), **revision from OAGB to RYGB** (4; 10%)	
Salminen 2018/SLEEVEPASS	RYGB	Early, major	**Bleeding** (7; 6%), intra-abdominal infection/infection of unknown origin (3; 2.6%), **torsion** of the entero-anastomosis (1; 0.9%)	
	SG		**Bleeding** (3; 2.5%), intra-abdominal infection/infection of unknown origin (1; 0.8%), pneumonia (1; 0.8%), bowel **perforation** (1; 0.8%), outlet **obstruction** (1; 0.8%)	
	RYGB	Early, minor	**Bleeding** (2; 1.7%), intra-abdominal infection/infection of unknown origin (8; 6.8%), pneumonia (6; 5.1%), superficial wound infection (3; 2.6%), dehydration (1; 0.9%)	
	SG		**Bleeding** (3; 2.5%), intra-abdominal infection/infection of unknown origin (2; 1.7%), pneumonia (1; 0.8%), superficial wound infection (2; 1.7%), troacar	

			site pain (1; 0.8%)	
	RYGB	Late, major	**Internal herniation** (17; 14.3%), incisional hernia (; 0.8%)1	
	SG		**GERD** (7; 5.8%), incisional hernia (3; 2.5%)	
	RYGB	Late, minor	Vomiting/dehydration (3; 2.5%), **ulcer/stricture** at gastrojejunal anastomosis (6; 5%), dumping (3; 2.5%), nonspecific abdominal pain (1; 0.8%)	
	SG		**GERD** (11; 9.1%), **ulcer/stricture** at gastrojejunal anastomosis (2; 1.7%)	
Schauer 2012; 2017/STAMPEDE	RYGB	Serious adverse event	**Transfusion** (1; 2%), Hemoglobin decrease ≥5 g/dl (1; 2%), Transient renal insufficiency (1; 2%), cholelithiasis (1; 2%)	*Schauer 2017 distinguished AEs by type, 2012 by "serious" and other*
	SG		**Transfusion** (1; 2%), arrythmia or palpitations (1; 2%), pleural effusion (1; 2%)	
	RYGB	Cardiovascular	-	
	SG		**Stroke** (1; 2%)	
	RYGB	Gastrointestinal	Bowel **obstruction** (1; 2%), **stricture** (1; 2%), ulcer (4; 8%), **bleeding** (2; 4%), **GERD** (5; 10%), dumping syndrome (4; 8%), gallstone diseases (1; 2%)	
	SG		Bowel **obstruction** (1; 2%), **stricture** (1; 2%), ulcer (1; 2%), **leak** (1; 2%), **GERD** (13; 27%), dumping syndrome (1; 2%), gallstone diseases (1; 2%)	
	RYGB	Urinary	Nephropathy (11; 22%), calculus (6; 12%)	
	SG		Nephropathy (9; 18%), calculus (5; 10%), incontinence (2;4%)	
	RYGB	Neurologic and psychiatric	Memory loss (1; 2%), neuropathy (1; 2%), depression (7; 14%)	
	SG		Memory loss (1; 2%), neuropathy (5; 10%), depression (12; 24%)	
	RYGB	Soft tissue and musculoskeletal	Hernia unspecified (3; 6%), **limb fracture** (4; 8%), foot ulcer (2; 4%)	
	SG		Hernia unspecified (1; 2%), **limb fracture** (3; 6%), foot ulcer (2; 4%)	
	RYGB	Nutritional and metabolic	Intravenous treatment for dehydration (7; 14%), **anemia (14; 28%),** hypoglycemic episode (32; 64%), Severe hypoglycemia requiring intervention (2;%), hyperglycemia (3; 6%), ketoacidosis (1; 2%)	
	SG		Intravenous treatment for dehydration (4; 8%), **anemia (24; 49%)**, hypoglycemic episode (40; 82%), hyperglycemia (3; 6%)	

	RYGB	Infectious	Wound infection (3; 6%), pneumonia (2; 4%)	
	SG		Wound infection (3; 6%), pneumonia (1; 2%), sepsis (1; 2%)	
	RYGB	Cancer	(2; 4%)	
	SG		(3; 6%)	
	RYGB	Late Major	-	
	SG		**Fistula** (1)	
Seetharamaiah 2017; Shivakumar 2018	SG	Early, Complication	**Hemorrhage** (4), **Leak** (1), **GERD** (3)	*AEs were not distinguished by major/minor but as complication/readmission*
	OAGB		**Hemorrhage** (3), Marginal Ulcer (2), **GERD** (2)	
	SG	Early, Reasons for readmission	12 in total (Bleeding (1), leak (1), nausea and vomiting (4), wound infection (6))	
	OAGB		10 in total (Bleeding (1), marginal ulcer perforation (1), marginal ulcer bleed (1), nausea and vomiting (3), wound infection (4))	
	SG	Late	Mortality (1), **revisions** (1), incidence of GSD (1)	
	OAGB		Mortality (1), incidence of GSD (3)	
Svanevik 2015[4]	RYGB	Peri/Postoperatively	-	*No deaths occurred*
	D-RYGB		**Leakage** from enteroenterostomy (1), **obstruction** of the enteroenteroanastomosis (1), iatrogenic small **bowel injury** (1), small bowel **obstruction** (2), intraabdominal **bleeding** (1)	
Svanevik2015; Risstad 2016	RYGB	Gastrointestinal	**Internal hernia** (5), gastrojujenal ulcer (2), small-bowel **obstruction** (1), incisional hernia (1), cholelithiasis (2), chronic abdominal pain (2), other (2)	*AEs categorised by type.*
	D-RYGB		**Incisional hernia** (3), acute liver failure (1), acute abdominal pain (1), chronic abdominal pain (3), diarrhea (4), nausea/vomiting (2), other (4)	
	RYGB	Nutritional	Protein-calorie malnutrition (1)	
	D-RYGB		**Protein-calorie malnutrition** (3), **anemia** (3), **severe vitamin deficiency** (3)	
	RYGB	Other	Hypoglycemia (1), urolithiasis (4), infectious disease (9), other (11)	
	D-RYGB		Hypoglycemia (5), urolithiasis (1), infectious disease (8), other (7)	
Tognoni 2015	SG	Early	**Bleeding** (1; 4%), gastric **stenosis** (1; 4%)	*No distinction between*

Gentileschi 2020	B-SG		**Bleeding** (1; 4%)	*minor/major and no late AEs reported. This study focused solely on postoperative AEs*
Wallenius 2020/CONTROL	RYGB	Intraoperative	Small bowel **perforation** (2), **obstruction** leading to a **redo** of their jejuno-jejunostomy (1)	*Early AEs were split into intra- and postoperative. No late AEs were recorded.*
	SG		**Bleeding** in the spleen (1; 4.2%), thick and inflamed gastric antrum leading to **conversion to RYGB** (1; 4.2%)	
	RYGB	Postoperative	-	
	SG		Staple-line **leak** at the proximal part of the sleeve (1), suspected intra-abdominal abscess (1)	
	RYGB	Late	-	
	SG		-	
Zhang 2014	RYGB	Early, Major	**Bleeding** (1), posterior **leak** (1)	
	SG		**Bleeding** (1)	
	RYGB	Early, Minor	-	
	SG		**Gastroesophageal reflux-GERD** (3; 9.34%)	
	RYGB	Late, Major	Gastro-jejunal **stenosis** (2), **internal hernia** (1)	
	SG		-	
	RYGB	Late, Minor	Severe dumping syndrome (2), hair loss (3)	
	SG		-	

1 Aasheim/Søvik/Risstad papers: uses different ways of categorizing AEs. 2 Courcoulas 2014, 2015 and 2020: Numbers, descriptions, and classification of AEs are inconsistent across studies. Overlap across studies with different follow-up. 3 Nguyen 2018 does not specify whether the numbers are in addition to the previous results or the total. this does not add up since some numbers for the same AEs from 2009 are larger. 4 Different language to describe the AEs in the studies that belong to the same trial.

List of planned, ongoing, withdrawn and completed studies without results

Table A25: List of planned, ongoing, withdrawn and completed studies without results with obesity surgery

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Relevant endpoints
NCT02882685	December 2026	RCT	120	OAGB	RYGB	Morbid obesity	Weight-loss [10y]
NCT03524365	September 2025	RCT	288	RYGB	SG	NASH	Adverse events [1y] Changes in glycemic control [1y] Changes in cardiovascular risk score [1y] Changes in insulin sensitivity [1y] Changes in quality of life [1y] NASH resolution [1, 3, 5y]
NCT03610256	October 2023	RCT	366	SADI	RYGB	Morbid obesity	Excess Weight Loss [2y] HbA1c [1, 3, 6, 12, 18, 24m] Fasting glycemia [1, 3, 6, 12, 18, 24m HDL [1, 3, 6, 12, 18, 24m] LDL [1, 3, 6, 12, 18, 24m] Cholesterol [1, 3, 6, 12, 18, 24m] Triglycerides [1, 3, 6, 12, 18, 24m]

							Antidiabetic drugs [6, 12, 24m] Antilipidemic drugs [6, 12, 24m] Antihypertensive drugs [6, 12, 24m] Length of stay [End of the hospitalization period] Readmission of patient [30d] Complications [2y] Weight loss [1, 3, 6, 12, 18, 24 m] Excess BMI Loss percentage [1, 3, 6, 12, 18, 24m]
NCT02841527	March 2023	RCT	1341	RYGB	AGB, SG	Morbid obesity	Excess weight loss > 50% [3y] Health-related Quality of Life [3y] Change in BMI [3y] Weight loss [3y] Adverse events [3y] Resolution of co-morbidities [3y]
NCT01778738	January 2023	RCT	125	SG	RYGB	T2D in Obese	Remission of type 2 diabetes [1y] Glycaemic control [5w to 5y] Insulin sensitivity [5w to 5y] Anti-diabetic medication [5w to 5y] Body weight [5w to 5y] Blood pressure [5w to 5y] Lipidemia [5w to 5y] Health related quality of life [5w to 5y] Vitamin and mineral deficiencies [5w to 5y]

NCT02767505	December 2022	RCT	2100	SG	RYGB	Severe obesity	Weight loss [1, 2, 5y] Serious adverse events [postop, 1, 2, 5y] Arterial cardiovascular events [1, 2 and 5y] Venous event [1, 2 and 5y] Diabetes requiring drug treatment [1, 2 and 5y] Hypertension [Baseline, 1, 2 and 5y] Dyslipidemia [Baseline, 1, 2 and 5y] Nutritional status [2 and 5y] Changes in quality of Life [Baseline, 1, 2 and 5y] Gastro-esophageal reflux disease [1, 2 and 5y] Mortality and cause of death [5, 10, 20 and 30 y] Development of co-morbidities [5, 10, 20, 30 y] Surgical time [Up to 30 days postop] Length of stay [Up to 30 days postop]
ChiCTR1800016455	June 2022	RCT	100	SG	RYGB	T2D in Obese	Glucose control Adverse events Weight Medication
NCT03891056	January 2022	RCT	40	RYGB	SG	T2D in Obese	Glycosylated hemoglobin levels [1y] Partial remission or improvement of diabetes [1y] Weight loss [2y] Postoperative complications

NCT03045679	December 2020 No publications with data found	RCT	100	OAGB	RYGB	T2D in Obese	Complications [2y] Mortality [2y] Remission of type 2 diabetes mellitus [2y] Remission of hypertonus [2y] Gastro-esophageal reflux disease [2y] Remission of sleep apnea [2y] Remission of hypertrigliceridemia [2y] Remission of hypercholesterinemia [2y] Quality of life questionnaire [2y] Weight loss [2y] Operation time [during surgery] Revisional surgery [2y]
NCT02601092	December 2020 No publications with data found	RCT	80	OAGB	RYGB	Morbid obesity	Excess Weight Loss [1y] Early complications [≤ 30d] Operation time [intraoperative] Length of stay [24w] Glucose homeostasis [6w, 1 and 3y] Lipid profile [6w, 1 and 3y]
NCT04134156	November 2019 No publications with data found	RCT	40	SG	OAGB	Morbid obesity	Excess weight loss [12m]
NCT02545647	September 2019 No publications with data found	RCT	130	B-RYGB	RYGB	Morbid Obesity	Percentage total body weight loss [3y] Percentage excess weight loss [3y] Percentage total body weight regain [3y] Type 2 diabetes mellitus [3y]

							Quality of life [3y] Dyslipidaemia [3y] Hypertension [3y]
NCT02290418	December 2018 No publications with data found	RCT	50	OAGB	RYGB	Morbid obesity	BAROS [1, 2y]
NCT03821688	August 2018 No publications with data found	RCT	210	SASJ	OAGB, SG	Morbid obesity	Percentage of excess weight loss [12m] Mutritional deficiency [2y] Improved co-morbidity [2y] Early operative complications [1m]
NTR4466	April 2018 No publications with data found	RCT	444	D-RYGB	RYGB	Morbid obesity	Percentage Excess Weight Loss [1y] Health-related quality of life [2, 6, 12m] Operating time Mean hospital stay Intra-operative and post-operative morbidity In-hospital mortality Improved co-morbidity
NCT02310555	May 2016 No publications with data found	RCT	90	RYGB	Modified RYGB, SG	T2 DM in Obese	Remission diabetes mellitus type II [2y] Weight loss [2y] Adverse effects [3m, 2y]
NCT01989988	December 2015 No publications with data found	RCT	60	OAGB	RYGB, SADJB	T2D in Obese	Remission of diabetes [2y] Weight loss Improvement in quality of life [2y]
NCT01015469	March 2015	RCT	384	B-RYGB	RYGB	Morbid Obesity	BMI [3, 6, 12m and 2, 3, 4, 5y]

	No publications with data found						
NCT01078181	May 2014 No publications with data found	RCT	100	RYGB	B-RYGB	Morbid Obesity	Excessive Weight Loss [3y]
ISRCTN33929407	2009 No publications with data found	RCT	Not provided	Gastric banding	RYGB	Obesity	Not provided
DRKS00000809	Withdrawn	RCT	70	B-SG	SG	Morbid Obesity	Excess body weight loss [3y] Safety of operation techniques [early and late, 5y] Adverse Incidents Quality of life [1, 3y] Changes in metabolic syndrome [5y] Changes in blood pressures [5y]
IRCT2013013112322N1	Not reported No publications with data found	RCT	290	RYGB	Gastric banding	Morbid obesity	Surgical complications [1w and 3, 6m]
U1111-1203-0901	Not reported No publications with data found	RCT	50	OAGB	RYGB	Morbid obesity	Excess weight loss Surgical morbidity
Almeida	Not reported	RCT	120	SADI-S	RYGB	Morbid obesity	Percentage excess weight loss [18m] Quality-of-life Improved comorbidity

							Early/late complications Malnutrition

Abbreviations: AGB: Adjustable Gastric Banding; B-RYGB: Banded RYGB; B-SG: Banded SG; D-RYGB: Distal RYGB; NASH: Non Alcoholic Steatohepatitis; OAGB: One Anastomosis Gastric Bypass; RCT: randomised controlled trial; RYGB: Roux-en-Y Gastric Bypass; SADI: Single-anastomosis Duodeno Ileal Bypass SADI-S: Single Anastomosis Duodenal Switch; SADJB: ; SASJ: Single anastomosis sleeve jejunal bypas; SG: Sleeve gastrectomy; T2D: Type 2 Diabetes Mellitus

Sources: ClinicalTrials.gov, WHO ICTRP, and EU Clinical Trials Register searched through Cochrane Central Register of Controlled Trials, Issue 5 of 12, May 2020.

Risk of bias tables and figures

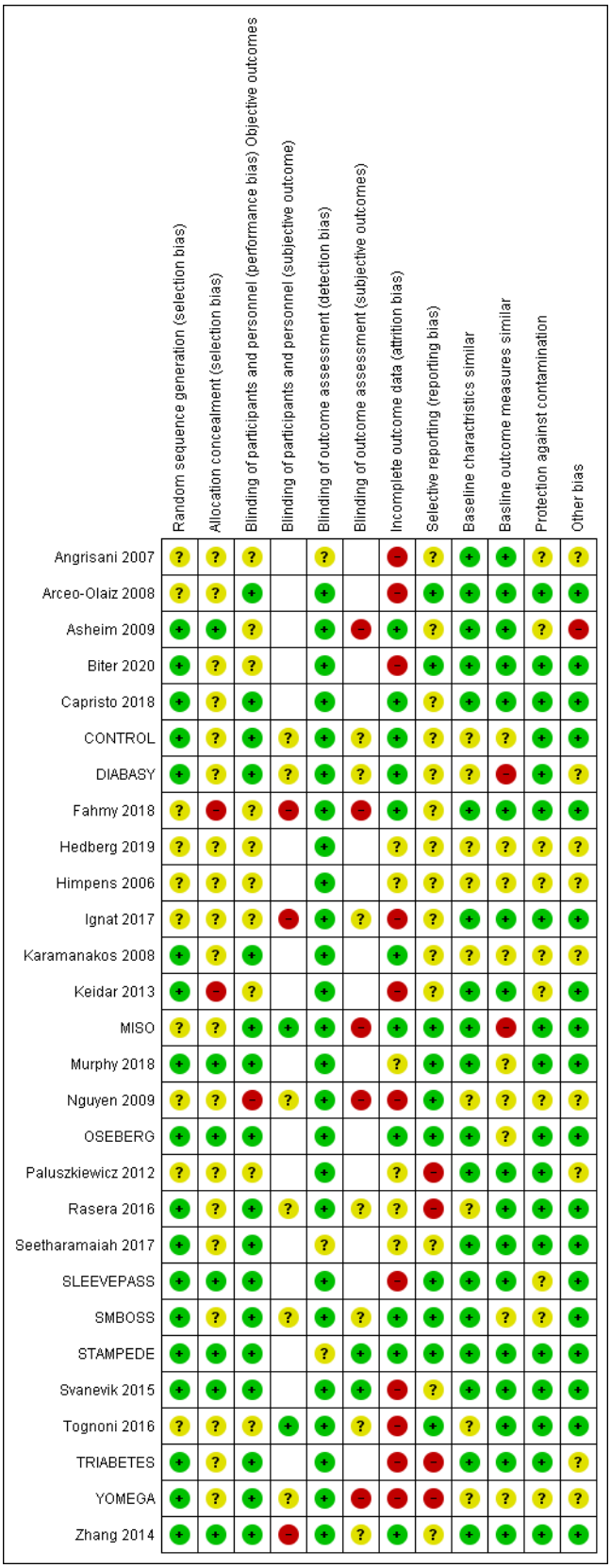

Figure A1: Risk of bias – study level (RCTs)

Footnote: Blank spots in domains related to blinding in Figure A1 above indicate that a particular study did not report any subjective outcomes.

Table A26: Risk of bias – study level (RCTs)

Trial (name, year, name)	Randomization sequence	Allocation concealment	Blinding		Incomplete outcome data	Selective outcome reporting	Other aspects increasing risk of bias	Overall Risk of bias – study level
			Participants and personnel	Outcome assessment - Objective outcome				
	AGB vs. RYGB							
Angrisani 2007	U (1)	U (2)	U (3)	L	H (4)	U (5)	L	H
Courcoulas 2014 - TRIABETES	L	U (2)	L	L	H (4)	H (6)	L	H
Nguyen 2009	U (1)	U (2)	U (7)	L	H (4,8)	U (5)	L	H
	AGB vs. SG							
Himpens 2006	U (1)	U (2)	L	L	U (9)	U (5)	U (10)	H
	SG vs. RYGB							
Biter 2020	L	U (2)	U (10)	L	H (4)	L	L	H
Capristo 2018	L	U (2)	L	L	L	H (6)	L	H
Hofsø 2019 – OSEBERG	L	L	L	L	L	L	L	L
Ignat 2017	U (1)	U (2)	U (3)	L	H (4)	H (5,6)	L	H
Karamanakos 2008	L	U (2)	L	L	L	U (5,11)	U (12)	H
Keidar 2013	L	H (13)	U (7)	L	H (14)	U (5)	L	H
Paluszkiewicz 2012	U (1)	U (2)	U (15)	L	U (16)	U (5,11)	U (10)	H
Peterli 2014 - SMBOSS	L	U (2)	L	L	L	U (5)	L	L
Salminen 2018 - SLEEVEPASS	L	L	L	L	H (17)	L	L	H
Schauer 2012 - STAMPEDE	L	L	L	L	L	L	L	L
Wallenius 2020 – CONTROL	L	U (2)	L	L	L	U (5)	L	U
Zhang 2014	L	U (2)	L	L	U (10)	U (5)	L	H
Svanevik 2015	L	L	L	L	H (4)	U (18)	L	H
	OAGB vs RYGB							
Fahmy 2018	U (1)	H (10)	L	L	L	U (5)	L	H
Robert 2019 – YOMEGA	L	U (2)	L	L	H (4)	H (6,18)	L	H
	OAGB vs. SG							
Seetharamaiah 2017	L	U (2)	L	L	U (4)	U (5)	L	H
	BPD-DS vs. RYGB							
Asheim 2009	L	L	U (10)	L	L	H (11)	H (19)	H
Hedberg 2012	U (1)	U (2)	U (3)	L	L	U (5)	U (20)	H

Mingrone 2012 - DIBASY	L	U (2)	L	L	L	L	L	L
	B-RYGB vs. RYGB							
Arceo-Olaiz 2008	U (1)	U (2)	U (10)	L	H (4)	U (5)	L	H
Rasera 2016	L	L	L	L	U (21)	H (5)	L	H
	B-RYGB vs. SG							
Murphy 2018	L	L	L	L	U (4)	L	L	L
	B-SG vs. SG							
Fink 2020 - MISO	U (1)	U (2)	U (3)	L	L	L	L	H
Tognoni 2016	U (1)	U (2)	U (10)	L	H (4)	U (5)	L	H

Footnotes: Unclear, Low Risk/High Risk

1. Insufficient details to assess how selection of participants (randomization) was done.
2. Insufficient details to assess how selection of participants (allocation) was done.
3. Open label trial (participants, personnel and outcome assessors aware of intervention) and unclear randomization
4. Attrition at follow-up (either large >20% or unexplained)
5. No protocol found; unable to judge
6. Differences found between protocol and full text publication
7. Participants were not blinded to the intervention
8. Proportion excluded immediately after randomisation differed notably between LRYGB and LAGB groups (11.2% and 31.2% respectively)
9. No discussion of any attrition or exclusions, appears to be no losses at 3 years but unable to check
10. Insufficient information to assess whether an important risk of bias exists
11. Outcome reporting inconsistencies between method and result sections
12. Supplementation was more extensive in LRYGB than LSG group
13. Allocation was not concealed
14. Unbalanced dropouts across groups
15. No details on blinding of participants and personnel
16. Conflicting information between abstract and full text; uncertainty over number of participants analysed
17. Different n for different measures and timepoints and almost 20% losses to Follow-up
18. Not all outcomes reported at follow-up
19. Between groups difference in nutritional supplementation
20. Additional unspecified intervention given to participants
21. Losses to follow-up not specified per group

Abbreviations: AGB: Adjustable Gastric Banding; BPD: BilioPancreatic Diversion; BPD-DS: Biliopancreatic Diversion with Duodenal Switch: B-RYGB: Banded Roux-en-Y Gastric Bypass; B-SG: Banded Sleeve Gastrectomy; D-RYGB: Distal Roux-en-Y Gastric Bypass; OAGB: One Anastomosis Gastric Bypass; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve Gastrectomy

Sources:

Table A27: Risk of bias – outcome level (RCTs)

[intervention vs intervention]	Endpoint Author, year	Study level	Blinding: outcome assessors	ITT principle adequately realized	Selective reporting of this outcome	Is the trial free from other outcome specific aspects	Overall RoB outcome specific level
	Mortality **Early mortality (early death - < 30 d after the initial procedure)**						
SG vs RYGB	Peterli 2014 - SMBOSS	L	Y	Y	Y	Y	L
BPD-DS vs RYGB	Hedberg 2012	H	Y	U (1)	U (2)	U (3)	H
B-RYGB vs RYGB	Rasera 2015	H	Y	N	U (4)	N (5)	H
	Late mortality (late death - >30 d after the initial procedure)						
AGB vs RYGB	Nguyen 2009, 2018	H	Y	Y	Y	U (6)	H
SG vs RYGB	Peterli 2014 - SMBOSS	L	Y	Y	Y	Y	L
SG vs RYGB	Salminen 2018 - SLEEVEPASS	H	Y	N	U (7)	Y	H
OAGB vs RYGB	Robert 2019 - YOMEGA	H	Y	N (8)	U (9)	N (10)	H
OAGB vs. SG	Seetharamaiah 2017	H	Y	N	U (11)	U (2)	H
BPD-DS vs RYGB	Aasheim 2009	H	Y	Y	Y	Y	H
B-RYGB vs. RYGB	Arceo-Olaiz 2008	H	Y	U (2)	U (7)	U (12)	H
B-RYGB vs RYGB	Rasera 2015	H	Y	N	U (4)	N (5)	H
	Morbidity						
	Weight Change						
AGB vs RYGB	Angrisani 2007	H	Y	N	Y	U (2)	H
AGB vs RYGB	Courcoulas 2014 -	H	Y	Y	Y	Y	H

	TRIABETES						
AGB vs RYGB	Nguyen 2009, 2018	H	Y	Y	Y	U (6)	H
AGB vs SG	Himpens 2006	H	Y	N	N (13)	U (2)	H
SG vs RYGB	Biter 2020	H	Y	N	N (14)	N (15)	H
SG vs RYGB	Salminen 2018 SLEEVEPASS	H	Y	N	U (7)	Y	H
SG vs RYGB	Ignat 2017	H	Y	N	Y	Y	H
SG vs RYGB	Peterli 2014 - SMBOSS	L	Y	N	Y	Y	L
SG vs RYGB	Schauer 2012 STAMPEDE	L	Y	Y	Y	Y	L
SG vs RYGB	Wallenius 2020/CONTROL	U	Y	N	Y	Y	U
SG vs RYGB	Zhang 2014	H	Y	Y	Y	Y	H
SG vs RYGB	Karamanakos 2008	H	Y	U	U (16)	Y	H
D-RYGB vs. RYGB	Svanevik 2015	H	Y	N	Y	U (2)	H
OAGB vs RYGB	Robert 2019 - YOMEGA	H	Y	N (8)	U (9)	N (10)	H
OAGB vs. SG	Seetharamaiah 2017	H	Y	N	U (11)	U (2)	H
BPD-DS vs RYGB	Hedberg 2012	H	Y	U (1)	U (2)	U (3)	H
BPD-DS vs RYGB	Mingrone 2012 - DIABASY	L	Y	Y	Y	Y	L
BPD-DS vs RYGB	Aasheim 2009	H	Y	Y	Y	Y	H
B-RYGB vs RYGB	Rasera 2015	H	Y	N	U (4)	N (5)	H
B-RYGB vs. RYGB	Arceo-Olaiz 2008	H	Y	U (2)	Y	U (2)	H
B-SG vs SG	Fink 2020 - MISO	H	Y	Y	Y	Y	H
B-SG vs SG	Tognoni 2013	H	Y	Y	Y	Y	H
	Diabetes						
AGB vs RYGB	Courcoulas 2014 - TRIABETES	H	L	Y	Y	Y	H
SG vs RYGB	Schauer 2012 - STAMPEDE	L	L	Y	Y	Y	Y
SG vs RYGB	Wallenius 2020 - CONTROL	U	L	N	Y	Y	U

SG vs RYGB	Salminen 2018 SLEEVEPASS	H	Y	N	U (7)	Y	H
D-RYGB vs. RYGB	Svanevik 2015	H	Y	N	Y	U (2)	H
OAGB vs RYGB	Robert 2019 - YOMEGA	H	Y	N (8)	U (9)	N (10)	H
OAGB vs. SG	Seetharamaiah 2017	H	Y	N	U (11)	U (2)	H
BPD-DS vs RYGB	Mingrone 2012 - DIABASY	L	L	Y	Y	L	L
BPD-DS vs RYGB	Hedberg 2012	H	Y	U (1)	U (2)	U (3)	H
B-SG vs SG	Fink 2020 - MISO	H	L	Y	Y	Y	H
	Health-related quality of life						
SG vs RYGB	Ignat 2017	H	H	N	Y	Y	H
SG vs RYGB	Peterli 2014 - SMBOSS	L	H	Y	Y	Y	L
SG vs RYGB	Salminen 2018 - SLEVEPASS	H	H	N	U (7)	Y	H
SG vs RYGB	Schauer 2012 - STAMPEDE	L	H	Y	Y	Y	Y
SG vs RYGB	Zhang 2014	H	H	Y	Y	Y	H
D-RYGB vs RYGB	Svanevik 2015	H	H	N	Y	U (2)	H
OAGB vs RYGB	Robert 2019- YOMEGA	H	H	N (8)	U (9)	N (10)	H
BPD-DS vs RYGB	Aasheim 2009	H	H	Y	U (15)	Y	H
BPD vs RYGB	Mingrone 2012 - DIABASY	L	H	Y	Y	Y	L
B-RYGB vs RYGB	Rasera 2015	H	H	N	U (4)	N (5)	H
B-SG vs SG	Fink 2020 - MISO	H	H	Y	Y	Y	H
Footnotes: Y-Yes, N-No, U-Unclear – L-Low Risk, H- High Risk							

1. No protocol
2. Not enough information to judge
3. Trial stopped early due to patients declining randomization; Interim analysis only
4. 5 deaths; 2/5 related to the procedure, and 3/5 non related but no further information provided
5. Use of inappropriate statistical methods
6. Excluded those who did not want to go through the study randomization
7. No per group death explanation given
8. Authors analysed the primary and secondary efficacy outcomes in the per-protocol population;
9. Timing and reasons for deaths not reported
10. People with major deviations from protocol were excluded
11. Death reasons reported for one group only (OAGB)
12. 17 participants lost to follow up, no explanation given'
13. No measures of dispersion
14. Authors report having more information but do not give numbers, no information for the procedures (only sweet/non sweet eaters)

15. Measure of dispersion lacking
16. Analysis not reported

Abbreviations: AGB: Adjustable Gastric Banding; BPD: BilioPancreatic Diversion; BPD-DS: Biliopancreatic Diversion with Duodenal Switch: B-RYGB: Banded Roux-en-Y Gastric Bypass; B-SG: Banded Sleeve Gastrectomy; D-RYGB: Distal Roux-en-Y Gastric Bypass; OAGB: One Anastomosis Gastric Bypass; RYGB: Roux-en-Y Gastric Bypass; SG: Sleeve Gastrectomy

Sources:

Applicability tables

Table A28: Summary table characterising the applicability of a body of studies

Domain	Description of applicability of evidence
Population	Twenty of the included studies involved participants with class 3 obesity, and of these four studies included people with super-obesity. Four studies included people with Class 2 obesity. Seven studies (4 EFF and 3 SAF) included participants with T2DM only. The other studies included varying number of participants with T2DM, and all studies included various proportions of participants with different co-morbidities at baseline (e.g. hypertension, dyslipidemia, sleep apnea, metabolic syndrome, and GERD). Among studies including participants with T2DM the duration of disease (when reported) was typically between 3 and 8 years, which may have affected the effectiveness of the intervention on diabetes remission. Results of two studies that included Asian populations, who are at a greater risk at a lower BMI, may not be applicable to a European obese populationp. There are no populations that are considered to have greater or lower baseline risk for benefits or harms. Where possible, describe the proportion with characteristics potentially affecting applicability (e.g.% over age 65) rather than the range or average.]
Intervention	A number of different surgical procedures to treat obesity were assessed in the included studies: AGB, SG, RYGB, D-RYGB, OAGB, BPD, and BPD-DS. In addition, a couple of procedures combined traditional procedures with rings or banding were evaluated. None of the studies assessed the effectiveness and safety of two more recently developed procedures: SASI or SADI-S. BPD, BPD-DS, and D-RYGB are procedures that nowadays are not very frequently used, and only for people with severe obesity.
Comparators	The comparators used were any of the procedures listed above, but most of the studies compared different surgical procedure with RYGB, which is considered the gold standard. It was not clear whether the other surgical procedure always reflected the best alternative treatment, or the best alternative treatment for a specific population.
Outcomes	All included studies reported one or more measure of weight loss/weight status, and 16 studies also reported on outcomes related to diabetes status and/or remission. Data for a number of outcomes were reported in less than half of the included studies (e.g. HRQOL, lipids, hypertension etc.). Follow-up for the EFF studies ranged from 2 to 10 years, but only two studies reported results data for follow-up that was longer than 5 years. Most studies reported on early and/or late mortality and/or other adverse events, but the adverse events were classified and reported in many different ways. Long-term follow-up was mostly lacking, which is a limitation when attempting to determine the superiority of bariatric surgery in the long run. While the main aim of obesity surgery is to decrease the risk of future cardiovascular events, factors related to cardiovascular risk reduction, was only reported in less than half of the studies. Even fewer studies reported on relapse of co-morbidities or weight re-gain.
Setting	The included studies were conducted at a total of 46 bariatric clinics or hospitals, of which a handful reported being high volume clinics. In most cases it was unclear if clinics were private or public. It is unclear if these clinics and hospitals, with a couple of exceptions, reflect the settings in which the intervention would typically be used. Eighteen studies were conducted in Europe, three in North America, two in south and central America, one in Oceania, one in Africa, and three in Asia.

Abbreviations: AGB: adjustable Gastric Banding; BPD: Biliopancreatic Diversion; BPD-DS: Biliopancreatic Diversion with Duopdenal Switch; D-RYGB: Distal Roux-en-Y Gastric Bypass; EFF: Effectiveness; GERD: Gastro Oesophageal Reflux Disease; HRQOL: Health-Related Quality of Life; OAGB: One Anastomosis Gastric Bypass; RYGB: Roux-en-Y Gastric Bypass; SAF: Safety; SADI-S: Single anastomosis duodeno-ileal bypass with sleeve; SASI: Single Anastomosis Sleeve Ileal Bypass; SG: Sleeve Gastrectomy

APPENDIX 2: REGULATORY AND REIMBURSEMENT STATUS

Due to missing data, and declining use of AGBs internationally [104], this table has not been completed. Information on regulatory status and indications for use retrieved from the websites of manufacturers of AGBs is presented in Table 11 “Indications for use and regulatory approval of adjustable gastric bands”.

APPENDIX 3: CHECKLIST FOR POTENTIAL ETHICAL, ORGANISATIONAL, PATIENT AND SOCIAL AND LEGAL ASPECTS

1. Ethical	
1.1. Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new ethical issues?	No
If answered with 'yes', please provide a short statement explaining why. *Example: Routine introduction of prenatal genetic screening tests, which could lead to pregnancy termination, may cause ethical issues for the couple as well as for the health-care provider.*	
1.2. Does comparing the new technology to the defined, existing comparators point to any differences that may be ethically relevant?	No
If answered with 'yes', please provide a short statement explaining why. *Example: The marketing authorisation holder claims that its product is superior, but has decided to limit the amount of the new medicine, which means that it has to be rationed and not all patients who need it can receive it. The comparator is freely available.*	
2. Organisational	
2.1. Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) require organisational changes?	No
If answered with 'yes', please provide a short statement explaining why. *Example: The new intervention requires the establishment of specialised centres for administration.*	
2.2. Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be organisationally relevant?	No
If answered with 'yes', please provide a short statement explaining why. *Example: The new technology will replace a surgical intervention, which may lead to excess capacity in relevant areas.*	
3. Social	
3.1. Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new social issues?	No
If answered with 'yes', please provide a short statement explaining why. *Example: A new technology allows patients to return to the workplace, but since the technology can be seen by co-workers, it may lead to stigmatisation.*	
3.2. Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be socially relevant?	No

If answered with 'yes', please provide a short statement explaining why. *Example: A technology, which is widely used by persons with abuse problems, colours the tongue blue, thus, immediately identifying the user. Comparators do not have this property.*	
4. Legal	
4.1. Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any legal issues?	No
If answered with 'yes', please provide a short statement explaining why. *Example: The comparator for the new technology is a pharmaceutical that is not licensed for the indication of concern, but is widely in use.*	
4.2. Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be legally relevant?	No
If answered with 'yes', please provide a short statement explaining why. *Examples:* • *The comparator for the new technology is a controlled, restricted substance, but the new medicine is not.* • *The most appropriate comparator for the new technology is available as a pharmacy-compounded medicine, but not as a finished product with marketing authorisation.* *Note: The assessment should not address patent-related issues.*	

APPENDIX 4: MISCELLANEOUS

Table A29: Documentation of queries to study authors in the assessment report

Study	Content of query	Reply received yes/no	Content of reply
NCT04134156	• The status of this trial • The estimated completion date • Any reports providing data for this study	No	No reply
NCT03821688	• The status of this trial	No	No reply
NCT02841527	• The estimated completion date	No	No reply
NTR4466	• Any reports providing data for this study	No	No reply
ISRCTN33929407	• The status of this trial	No	No reply
RBR-59k78k	• The estimated completion date	No	No reply
Irct2013013112322N	• Any reports providing data for this study	No	No reply
NCT03524365	• The status of this trial	Yes	Estimated completion date provided
NCT0254564	• The estimated completion date	No	No reply
NCT01078181	• Any reports providing data for this study	No	No reply
NCT01015469	• The status of this trial	No	No reply
Angrisani	• Missing data on weight outcomes • Inconsistencies in reported data for adverse events	No	No reply
Courcoulas	• Information on no of patients available for follow-up for different outcome measures.	Yes	Additional data provided
Hedberg	• Missing information about number of patients with diabetes at baseline.	No	No reply
Ignat	▪Missing information on comorbidity.	No	▪No reply
Lee	▪Wrong data for one of two outcomes.	No	▪No reply
Leeman/Biter	▪Missing data for BMI, and other outcomes	No	▪E-mail bounced
Leeman/Biter	▪Missing information on losses to follow-up.	No	▪E-mail bounced
Lorentzon 2019	▪Inquiry about possibly available full text.	No	▪No reply
Medina 2019	▪Could not find contact details		▪
Moustafa 2018	▪Could not find contact details		▪
Nguyen	▪Missing information on no of patients with comorbidity.	No	▪No reply

Omar 2019	▪Inquiry about possibly available full text.	No	▪No reply
Om Tantia	▪Unclear results tables, lacking explanatory footnotes.	No	▪No reply
Ospanov 2019	▪Inquiry about possibly available full text.	No	▪No reply
Peterli	▪Differences in means provided between various reports ▪Variance statistics for various outcomes ▪Access to supplemental files	Yes	▪Supplement file and additional data provided ▪In case of inconsistent values, the data from the JAMA paper should be used
Pucci 2015	▪Inquiry about possibly available full text.	No	▪No reply
Risstad	▪Missing data, and discrepancies between results in text and tables.	Yes	▪Additional data and clarifications received.
Risstad	▪Discrepancies between baseline outcomes in first and last trial publication.	Yes	▪Clarifications received.
Roberts	▪Information on where to find the trial protocol.	No	▪No reply
Ruiz 2017	▪Inquiry about possibly available full text.	No	▪No reply
Salminen	▪Additional results data.	Yes	▪Additional data provided
Saarinen 2019	▪Inquiry about possibly available full text.	No	▪No reply
Singh 2019	▪Could not find contact details		▪
Tan 2019	▪Could not find contact details		▪
Techagumpuch	▪Could not find contact details		▪
Troung 2018	▪Could not find contact details		▪
Wallenius	▪Clarification regarding randomisation of patients.	Yes	▪Clarification received.
Yashkov 2018	▪Could not find contact details		▪
Zhang	▪Missing information on patient baseline characteristics.	No	▪No reply
Garcia-Oria 2019	▪Availability of full report	No	▪ No reply
Welbourn 2019	▪Availability of full report	Yes	▪Not published
Alarcon 2019	▪Availability of full report	No	▪ No reply
Albanapoulos 2013	▪Availability of full report	No	▪ No reply
Almeida 2017	▪Availability of full report	No	▪ No reply
Bedi 2017	▪Availability of full report	No	▪ No reply
Berends 2019	▪Availability of full report	No	▪ No reply
Bhandarwar 2017	▪Availability of full report	No	▪ No reply
Casajoana 2019	▪Availability of full report	No	▪ No reply
Elkeleny 2017	▪Availability of full report	No	▪ No reply
Elkeleny 2017	▪Availability of full report	No	▪ No reply
Elkeleny 2018	▪Availability of full report	No	▪ No reply
Finno 2019	▪Availability of full report	No	▪ No reply
Gadiot 2017	▪Availability of full report	No	▪ No reply
Garcia Ruiz De Gordejuela 2015	▪Availability of full report	No	▪ No reply

Gentileschi 2019	▪Availability of full report	No	▪ No reply
Gomez Almendros 2019	▪Availability of full report	No	▪ No reply
Kraljevic 2017	▪Availability of full report	No	▪ No reply

For the purpose of transparency, a separate document with comments on the 2nd draft assessment from external experts and the manufacturer(s) (fact check), as well as responses from the author, is available on the EUnetHTA website.

Table A30: Studies (N=25) with more than 5 years follow-up reporting on adverse and hospital resource use after various types of bariatric surgery

Referanse	Land	Study type	Procedure	Patient Population, BMI and comorbidities	No of pts.	Readmission or reoperation	Adverse events	Length of follow-up
Abd Ellatif, M. E.; Abdallah, E. et al Long term predictors of success after laparoscopic sleeve gastrectomy International Journal Of Surgery - Volume 12, Issue 5, pp. 504-8 (2014)	Egypt	Retrospective study	SG	BMI: 46 kg/m2	1395	Revision surgery	Post-operative leaks, mortality	Mean follow-up 76 +/- 19 (range: 6-103) months
Almuhanna, M.; Soong, T. C. et al. Twenty years' experience of laparoscopic 1-anastomosis gastric bypass: surgical risk and	Taiwan	Retrospective analysis of a prospective bariatric database	OAGB	BMI: 40.2 +/- 11.9 kg/m2	739	Revision surgery	malnutrition	10, 15 years

long-term results Surgery for Obesity & Related Diseases - Volume 17, Issue 5, pp. 968-975 (2021)								
Angrisani, L.; Ferraro, L. et al. Long-term results of laparoscopic Roux-en-Y gastric bypass for morbid obesity: 105 patients with minimum follow-up of 15 years Surgery for Obesity & Related Diseases - Volume 17, Issue 4, pp. 727-736 (2021)	Italy	Retrospective analyses of a prospectively maintained database	RYGB	BMI: 47.2 +/- 6.4 kg/m2	105	Re-operations	postoperative nutrition status	15 years
Aarts, E. O.; Dogan, K. et al. Long-term results after laparoscopic adjustable gastric banding: a mean fourteen year follow-up study Surgery for Obesity & Related Diseases - Volume 10, Issue 4, pp. 633-40	Netherlands	Retrospective study	AGB	Morbid obesity	201	Reoperations		Mean 14 years

(2014)								
Carandina, S.; Soprani, A.; Zulian, V.; Cady, J.; Long-Term Results of One Anastomosis Gastric Bypass: a Single Center Experience with a Minimum Follow-Up of 10 Years Obesity Surgery - Volume 7, Issue 0, pp. 07 (2021)	France	Retrospectively reviewed of prospectively collected data	OAGB	Morbid obesity	385	Re-hospitalized for major malnutrition and anemia	Ulcer,	10 years, mean 149 months
Carlsson, L. M. S.; Sjoholm, K.; et al. Long-term incidence of serious fall-related injuries after bariatric surgery in Swedish obese subjects International Journal of Obesity - Volume 43, Issue 4, pp. 933-937 (2019)	Sweden	Prospective, controlled cohort	RYGB, banding, vertical banded gastroplasty	BMI:>= 34 kg/m2 in men and >=38 kg/m2 in women	2007		Falls	Median 19 years
Casella, G.; Soricelli, E.; et al. Long-term results after laparoscopic sleeve gastrectom	Italy	Retrospective study	SG	BMI: 45.9+/-7.3 kg/m2	182		GERD	6, 7 years

y in a large monocentric series Surgery for Obesity & Related Diseases - Volume 12, Issue 4, pp. 757-762 (2016)								
Castagneto Gissey, L.; Casella Mariolo, J. R et al 10-year follow-up after laparoscopic sleeve gastrectomy: Outcomes in a monocentric series Surgery for Obesity & Related Diseases - Volume 14, Issue 10, pp. 1480-1487 (2018)	Italy	Retrospective study	SG	Morbid obesity	182		GERD, co-morbidity	Minimum 10 years
Catoi, A. F.; Galea, R. F. et al. Weight Loss and Late Complications after Silastic Ring Vertical Gastroplasty. A 10 Year Follow-up. Chirurgia (Bucuresti) - Volume 114, Issue 6, pp. 761-	Romania	Retrospective cohort	Silastic Ring Vertical Gastroplasty	Severe obesity	112	Reoperations	Late surgical complications	10 years

768 (2019)								
El-Kadre, L.; Tinoco, A. C. et al. Overcoming the learning curve of laparoscopic Roux-en-Y gastric bypass: a 12-year experience Surgery for Obesity & Related Diseases - Volume 9, Issue 6, pp. 867-72 (2013)	Brazil	Retrospective study	RYGB	BMI: 45.15 kg/m2	2281	Conversion rate	Mortality	12 years
Gronroos, S.; Helmio, M.; et al. Effect of Laparoscopic Sleeve Gastrectomy vs Roux-en-Y Gastric Bypass on Weight Loss and Quality of Life at 7 Years in Patients With Morbid Obesity: The SLEEVEPASS Randomized Clinical Trial JAMA Surgery - Volume 156, Issue 2, pp. 137 - 146 (2021)	Finland	Multicenter, multisurgeon, open-label, randomized clinical equivalence trial	SG, LRYGB	BMI: 45.9 kg/m2 [6.0]	240		Morbidity	7 years
Guimaraes, M.; Osorio,	Brazil	Retrospective	RYGB	BMI: 44.4 +/-	28	Revision	Death	10

C. et al. How Sustained is Roux-en-Y Gastric Bypass Long-term Efficacy?: Roux-en-Y Gastric Bypass efficacy Obesity Surgery - Volume 22, Issue 0, pp. 22 (2021)		observational cohort		6.1 kg/m2	1	surgery		years
Hjorth, S.; Naslund, I.; et al.; Reoperations After Bariatric Surgery in 26 Years of Follow-up of the Swedish Obese Subjects Study JAMA Surgery - Volume 154, Issue 4, pp. 319-326 (2019)	Sweden	Prospective non-randomised controlled study	Banding, VBG, GBP.	BMI values of 34 kg/m2, women with BMI > 38 kg/m2	376		Band-associated complications, postsurgical morbidity	26 years
Kowalewski, P. K.; Olszewski, R. et al. Long-Term Outcomes of Laparoscopic Sleeve Gastrectomy-a Single-Center, Retrospective Study Obesity Surgery - Volume 28, Issue 1, pp.	Poland	Retrospective Study	SG	BMI: 51.6 kg/m2	127	Revisional surgery	GERD	Median 8.0 years

130-134 (2018)								
Kular, K. S.; Manchanda, N.; Cheema, G. K.; Seven Years of Mini-Gastric Bypass in Type II Diabetes Patients with a Body Mass Index <35 kg/m(2) Obesity Surgery - Volume 26, Issue 7, pp. 1457-62 (2016)	India	Prospectively collected data were analysed retrospectively	OAGB	BMI: 33.4 +/- 3.3 kg/m2 and T2D	128		Death, major complications	7 years
Malisev, E.; Ten-Year weight loss evaluation after adjustable gastric banding in severely and morbidly obese patients Journal of Gastroenterology and Hepatology Research - Volume 5, Issue 3, pp. 2093-2095 (2016)	France	Uni-centre retrospective study	AGB	BMI: 43.02 +/- 5.7 kg/m2	97	Band removal		10 years
Pontiroli, A. E.; Zakaria, A. S et al Long-term mortality and incidence	Italy	Matched cohort	gastric banding	Morbidly obese	385	Hospital admissions	Mortality	10, 15 years

of cardiovascular diseases and type 2 diabetes in diabetic and nondiabetic obese patients undergoing gastric banding: a controlled study Cardiovascular Diabetology - Volume 15, Issue 0, pp. 39 (2016)								
Sheikh, L.; Pearless, L. A.; Booth, M. W.; Laparoscopic Silastic Ring Mini-Gastric Bypass (SR-MGBP): Up to 11-Year Results from a Single Centre Obesity Surgery - Volume 27, Issue 9, pp. 2229-2234 (2017)	New Zealand	Cohort	Laparoscopic Silastic Ring OAGB	BMI: 46 kg/m2	156	Conversion	Death, anti-reflux medications	Up to 11 years
Stol, A.; Dadan, D. D.; et al Long follow-up of patients with gastric band Arquivos Brasileiros	Brazil	Case series	AGB	BMI: 41.95 kg/m2	19	Band redrawal	GERD	

de Cirurgia Digestiva - Volume 26, Issue 0, pp. 13-6 (2013)								
Strain, G. W.; Torghabeh, M. H. et al The Impact of Biliopancreatic Diversion with Duodenal Switch (BPD/DS) Over 9 Years Obesity Surgery - Volume 27, Issue 3, pp. 787-794 (2017)	USA	Cohort	BPD-DS	BMI: 53.4 kg/m2	284	Complications requiring surgery	Nutritional problems	9 years
Suter, M.; Mantziari, S. et al. Long-term results after Roux-en-Y gastric bypass for severe obesity Therapeutische Umschau - Volume 76, Issue 3, pp. 143-149 (2019)	Switzerland	Review prospective database	RYGB	Severe obesity	822		Comorbidities	10, 15 years
Topart, P.; Becouarn, G.; Delarue, J.; Weight Loss and Nutritional Outcomes 10 Years after Biliopancreatic	France	Cohort	BPD-DS	BMI:48.9 +/- 7.3 kg/m2	80	Revision	Vitamin	141 +/- 16months

Diversion with Duodenal Switch Obesity Surgery - Volume 27, Issue 7, pp. 1645-1650 (2017)								
Victorzon, M.; Tolonen, P.; Mean fourteen-year, 100% follow-up of laparoscopic adjustable gastric banding for morbid obesity Surgery for Obesity & Related Diseases - Volume 9, Issue 5, pp. 753-7 (2013)	Finland	Retrospective study	AGB	Morbid obesity	60	Reoperations	mortality	14.1 years (13.2-16.8 years)
Vitiello, A.; Berardi, G.; et al: Should Sleeve Gastrectomy Be Considered Only as a First Step in Super Obese Patients? 5-Year Results From a Single Center Surgical Laparoscopy, Endoscopy & Percutaneo	Italy	Retrospective analysis of a prospectively maintained database	SG	BMI: 57.4+/-5.8 kg/m2	66		GERD	More than 5 years

us Techniques - Volume 31, Issue 2, pp. 203-207 (2020)								
Vitiello, A.; Vincenzo, P.; et al. Ten years of follow-up of bilio-intestinal bypass: is malabsorption necessary for long-term metabolic results? Langenbecks Archives of Surgery - Volume 403, Issue 7, pp. 873-879 (2018)	Italy	Retrospective review	bilio-intestinal bypass	BMI 49.8 +/- 15.5 kg/m2	86	Reoperation rate	Mortality	10 years

APPENDIX 5: SUPPLEMENTARY NMA RESULTS

WEIGHT -2 YEARS NMA RESULTS -FIXED EFFECT

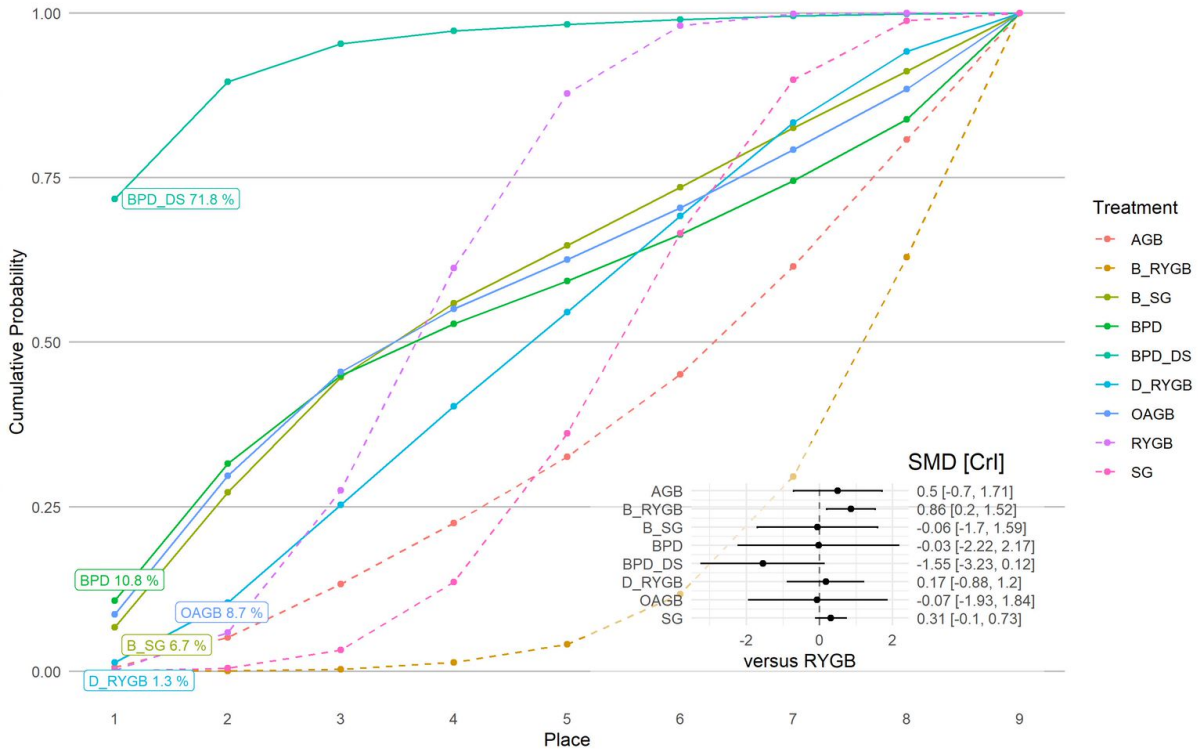

Figure A2: Sucra plot SMD weight outcome at 2 years follow-up (fixed effect)

SUCRA (colored plot): Treatments are displayed according to their probability to achieve a specific rank (or better). In specific, BPD_DS has a 65.7% probability to rank first and BPD a 9.5% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual treatments might achieve a high ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is only judged to be relevant if the credibility intervals of the forest plots show superiority.

Abbreviations: AGB: adjustable gastric banding; B_RYGB: band to Roux-en-Y gastric bypass; B_SG: banded sleeve gastrectomy; BPD: biliopancreatic diversion; BPD_DS: biliopancreatic diversion with duodenal switch; D_RYGB: distal Roux-en-Y gastric bypass; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy; SR_RYGB: silastic ring Roux-en-Y gastric bypass

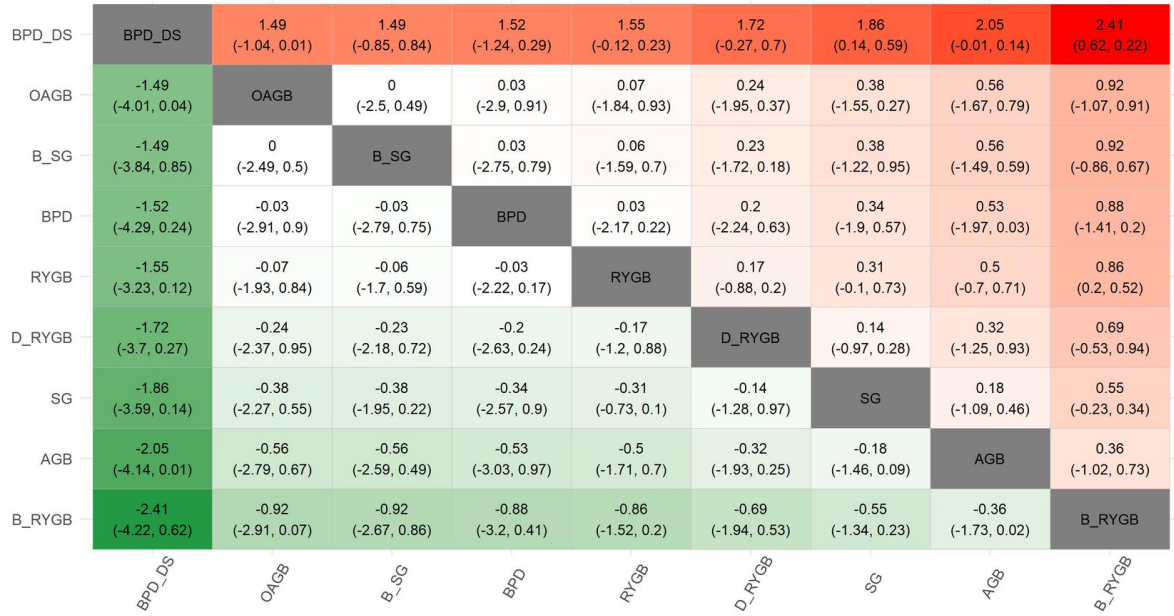

Figure A3: Heat map-SMD weight outcome at 2 years follow-up (fixed effect)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: AGB: adjustable gastric banding; B_RYGB: band to Roux-en-Y gastric bypass; B_SG: banded sleeve gastrectomy; BPD: biliopancreatic diversion; BPD_DS: biliopancreatic diversion with duodenal switch; D_RYGB: distal Roux-en-Y gastric bypass; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy; SR_RYGB: silastic ring Roux-en-Y gastric bypass

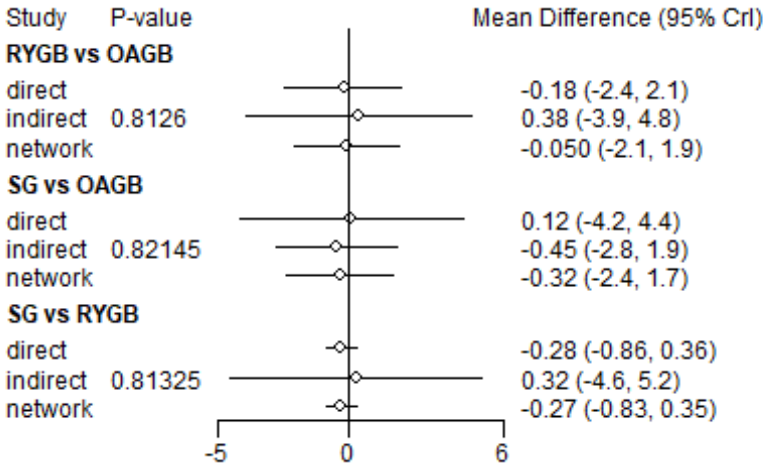

Figure A4: Nodesplit SMD weight outcome at 2 years follow-up (fixed effect)

WEIGHT -2 YEARS NMA RESULTS- RANDOM EFFECT

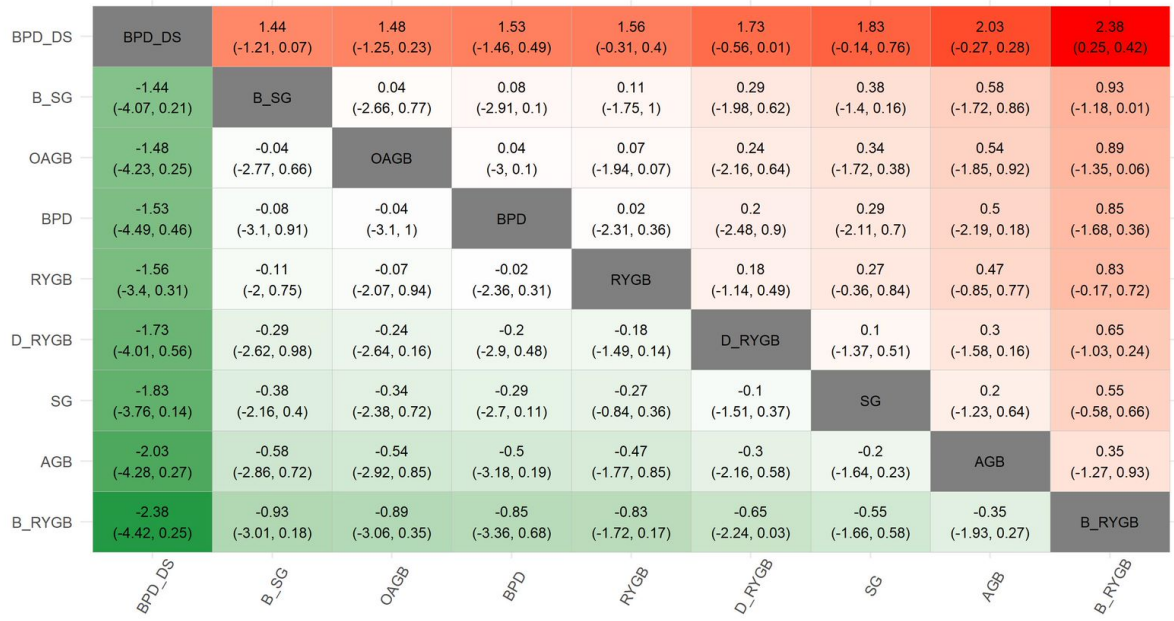

Figure A5: Heatmap SMD weight outcome at 2 years follow-up (random effect)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: AGB: adjustable gastric banding; B_RYGB: band to Roux-en-Y gastric bypass; B_SG: banded sleeve gastrectomy; BPD: biliopancreatic diversion; BPD_DS: biliopancreatic diversion with duodenal switch; D_RYGB: distal Roux-en-Y gastric bypass; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy; SR_RYGB: silastic ring Roux-en-Y gastric bypass

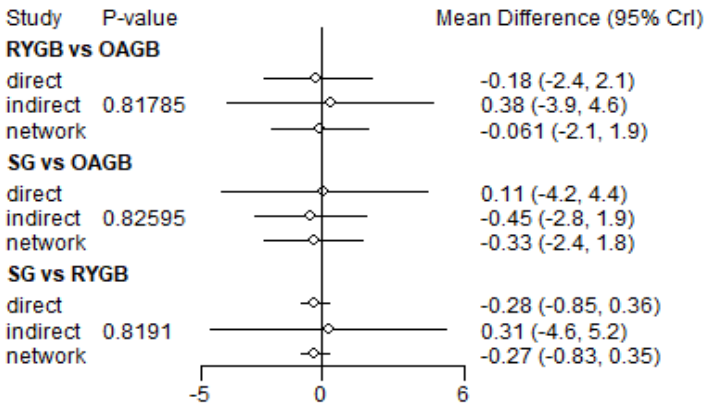

Figure A6: Nodesplit SMD weight outcomes at 2 years follow-up (random effect)

WEIGHT -3 YEARS NMA RESULTS- WEIGHT- FIXED EFFECT

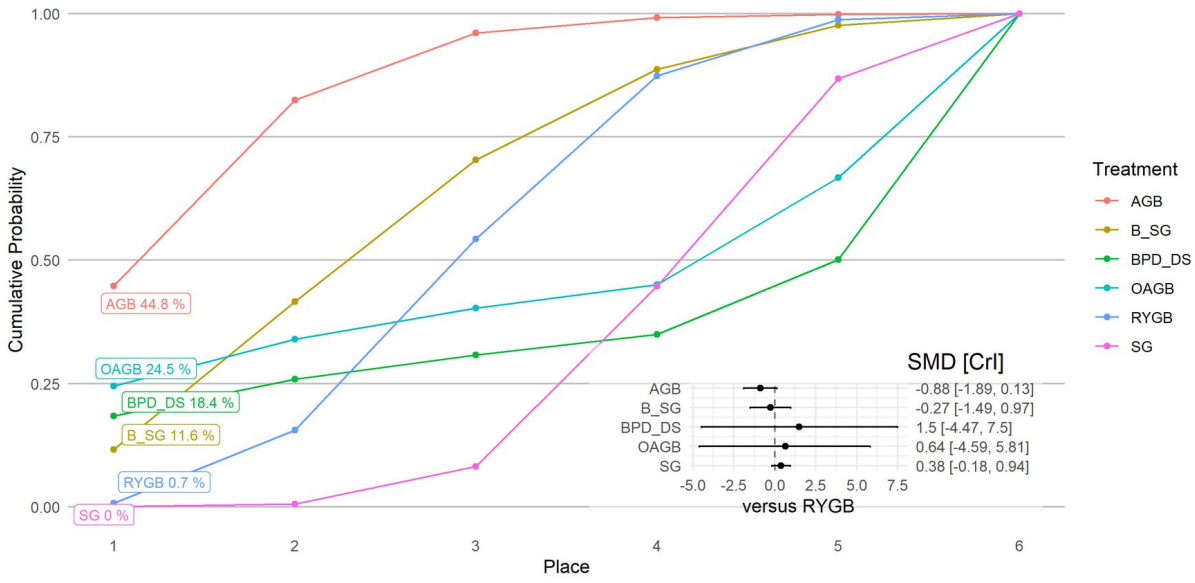

Figure A7: SUCRA SDM weight outcome at 3 years follow-up (fixed effect)

SUCRA (colored plot): Treatments are displayed according to their probability to achieve a specific rank (or better). In specific, AGB has 61.5% probability to rank first and OAGB a 19.5% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual treatments might achieve a high ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is only judged to be relevant if the credibility intervals of the forest plots show superiority.

Abbreviations: AGB: adjustable gastric banding; B_SG: banded sleeve gastrectomy; BPD_DS: biliopancreatic diversion with duodenal switch; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

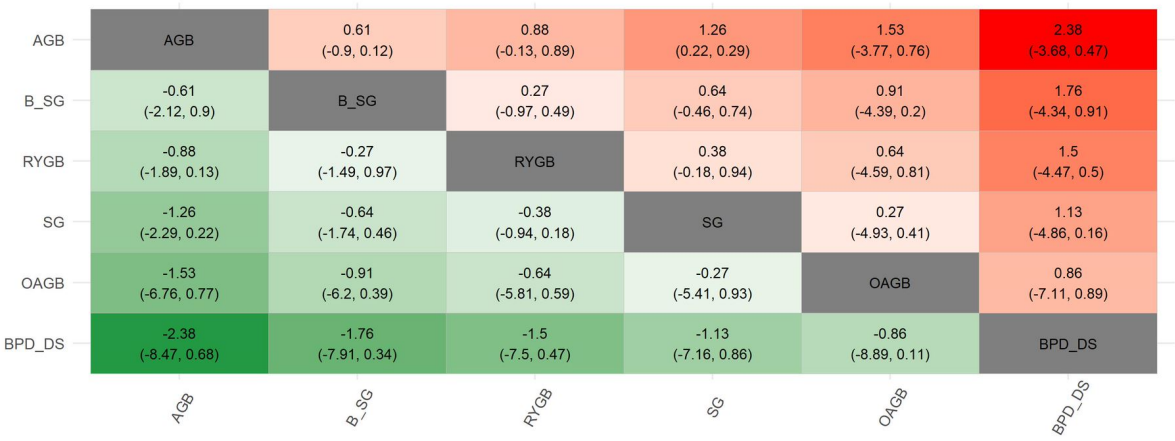

Figure A8: Heatmap SMD weight outcomes at 3 years follow-up (fixed effect)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: AGB: adjustable gastric banding; B_SG: banded sleeve gastrectomy; BPD_DS: biliopancreatic diversion with duodenal switch; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

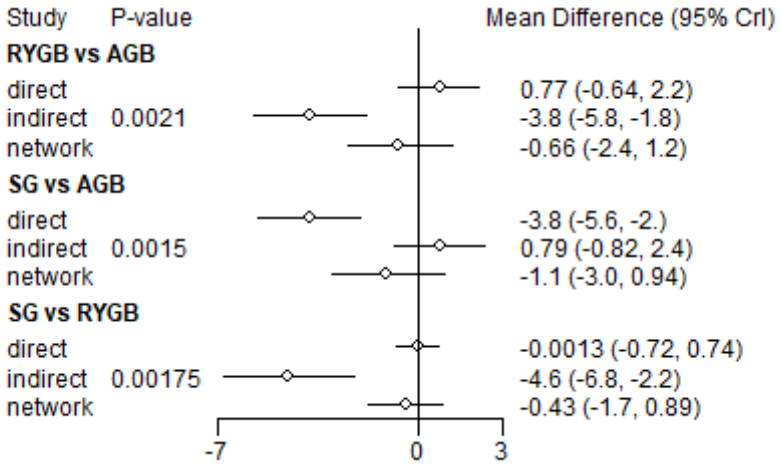

Figure A9: Nodesplit SMD weight outcome at 3 years (fixed effect)

WEIGHT - 3 YEARS NMA RESULTS- RANDOM EFFECT

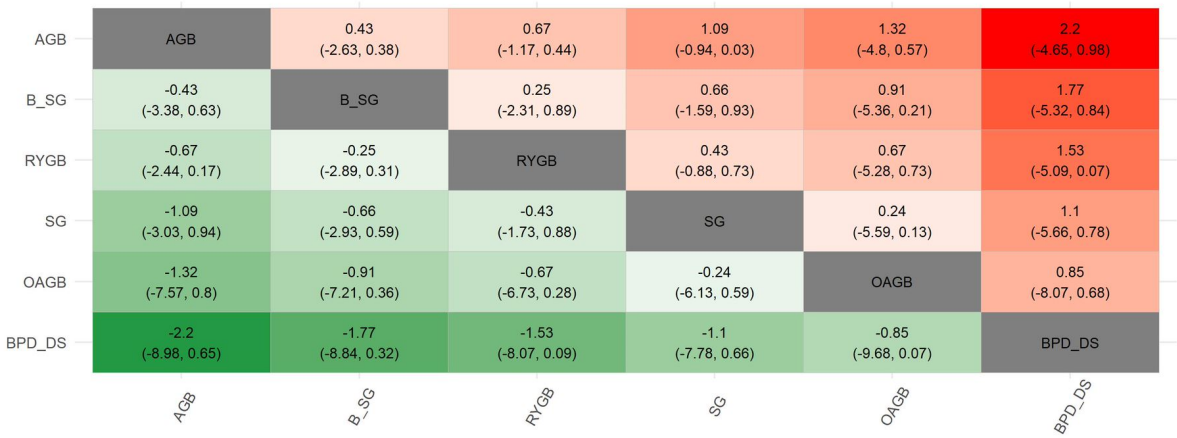

Figure A10: Heatmap SMD weight outcome at 3 years follow-up (random effect)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: AGB: adjustable gastric banding; B_SG: banded sleeve gastrectomy; BPD_DS: biliopancreatic diversion with duodenal switch; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

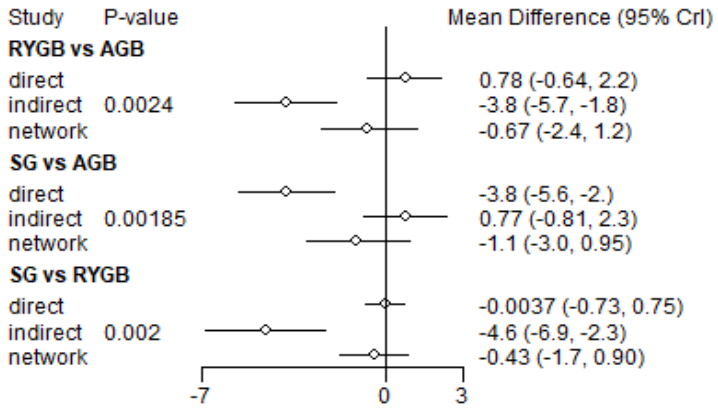

Figure A11: Nodesplit SMD weight outcome at 3 years follow-up (random)

WEIGHT - 5 YEARS NMA RESULTS - WEIGHT- FIXED EFFECT

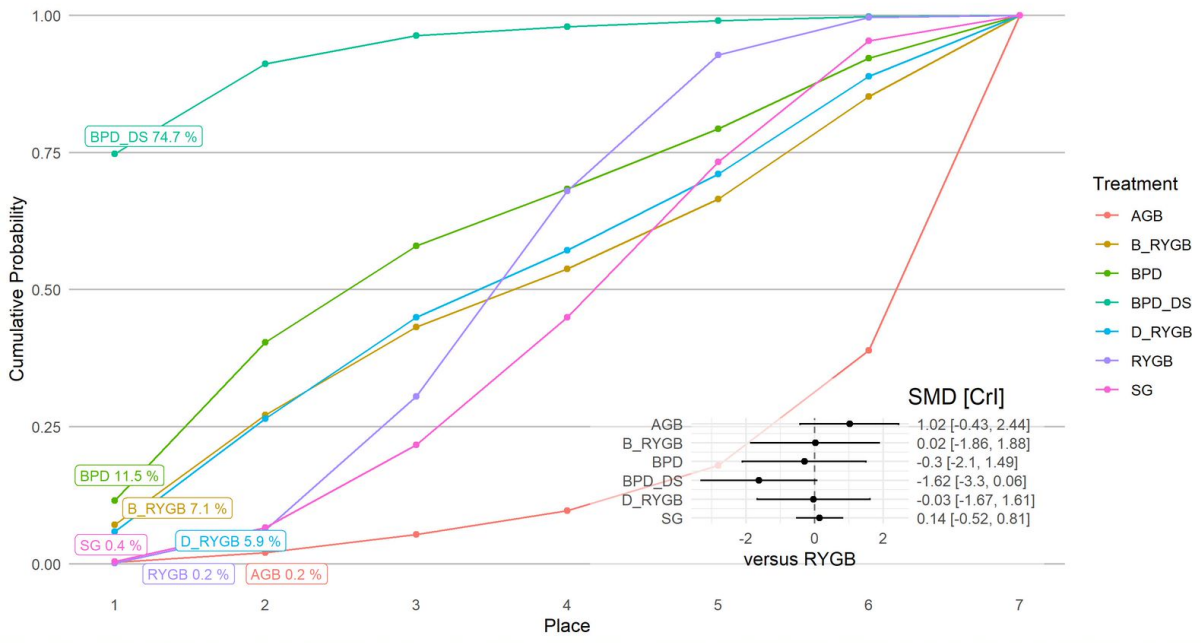

Figure A12: Sucra SMD weight outcomes at 5 years follow-up (fixed effect)

SUCRA (colored plot): Treatments are displayed according to their probability to achieve a specific rank (or better). In specific, BPD-DS has73% probability to rank first and BPD a 11.2% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual treatments might achieve a high ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is only judged to be relevant if the credibility intervals of the forest plots show superiority.

Abbreviations: AGB: adjustable gastric banding; B_RYGB: band to Roux-en-Y gastric bypass; BPD: biliopancreatic diversion; BPD_DS: biliopancreatic diversion with duodenal switch; D_RYGB: distal Roux-en-Y gastric bypass; LAGB: laparoscopic adjustable gastric banding; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

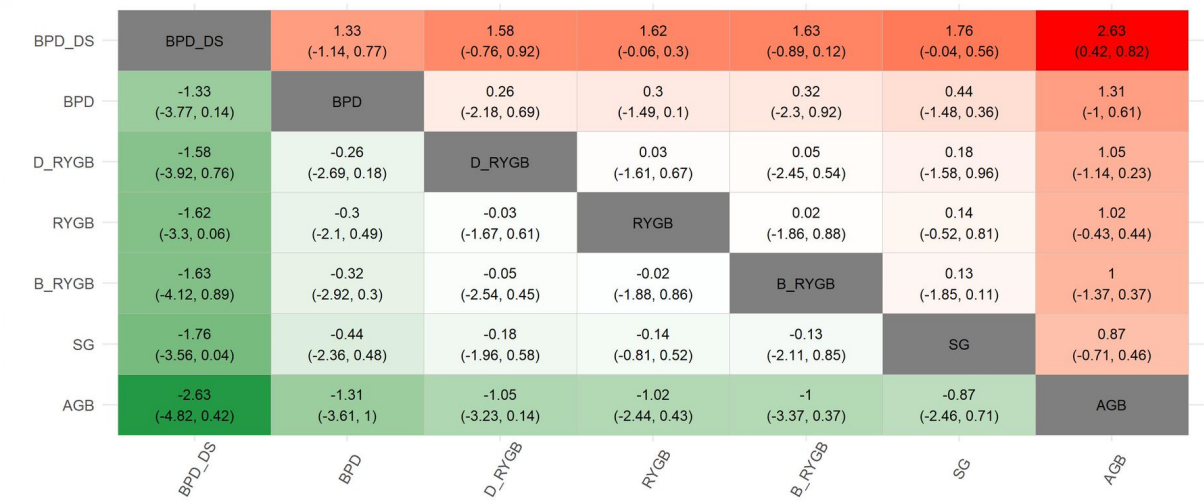

Figure A13: Heatmap SMD weight outcomes at 5 years follow-up (fixed effect)

WEIGHT - 5 YEARS NMA RESULTS- RANDOM EFFECT

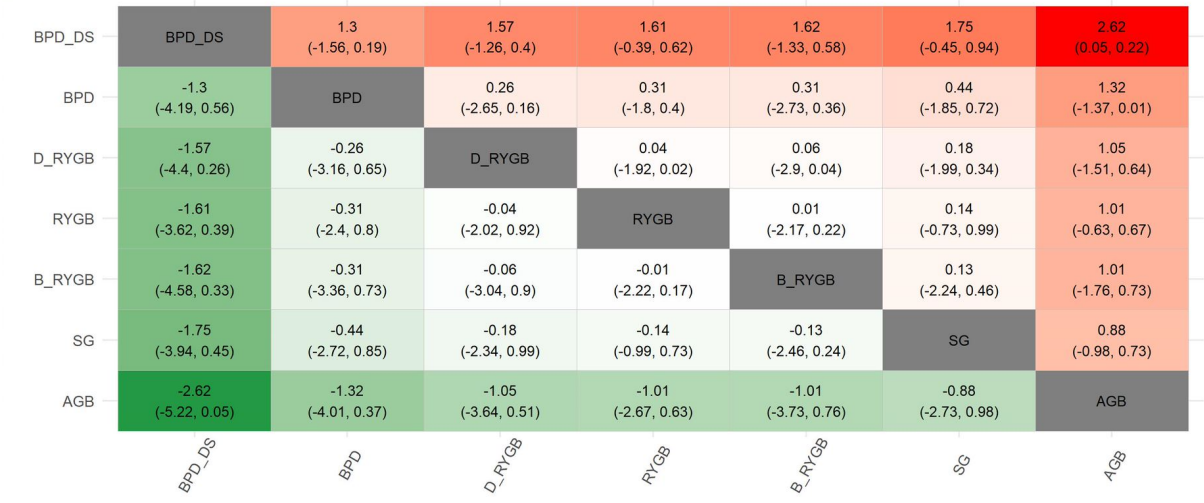

Figure A14: Heatmap SMD weight outcome at 5 years follow-up (random effect)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: AGB: adjustable gastric banding; B_RYGB: band to Roux-en-Y gastric bypass; BPD: biliopancreatic diversion; BPD_DS: biliopancreatic diversion with duodenal switch; D_RYGB: distal Roux-en-Y gastric bypass; LAGB: laparoscopic adjustable gastric banding; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

DIABETES 2 YEARS NMA RESULTS - FIXED EFFECT

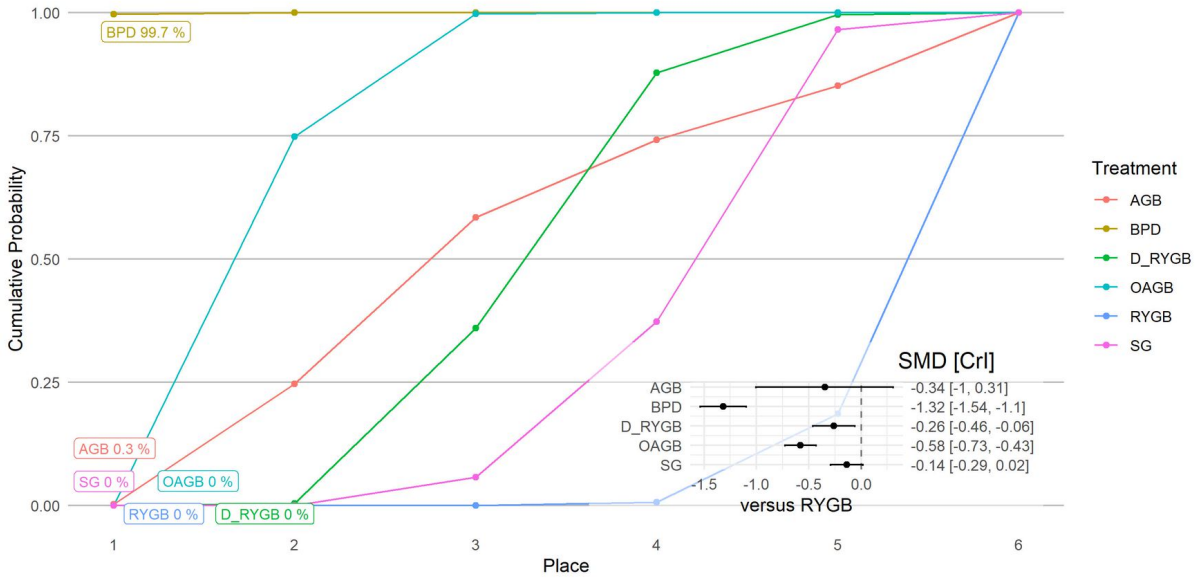

Figure A15: SUCRA plot SMD diabetes outcomes at 2 years follow-up (fixed effect)

SUCRA (colored plot): Treatments are displayed according to their probability to achieve a specific rank (or better). In specific, BPD has 99.7% probability to rank first and LAGB a 032% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual treatments might achieve a high ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is only judged to be relevant if the credibility intervals of the forest plots show superiority.

Abbreviations: BPD: biliopancreatic diversion; D_RYGB: distal Roux-en-Y gastric bypass; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

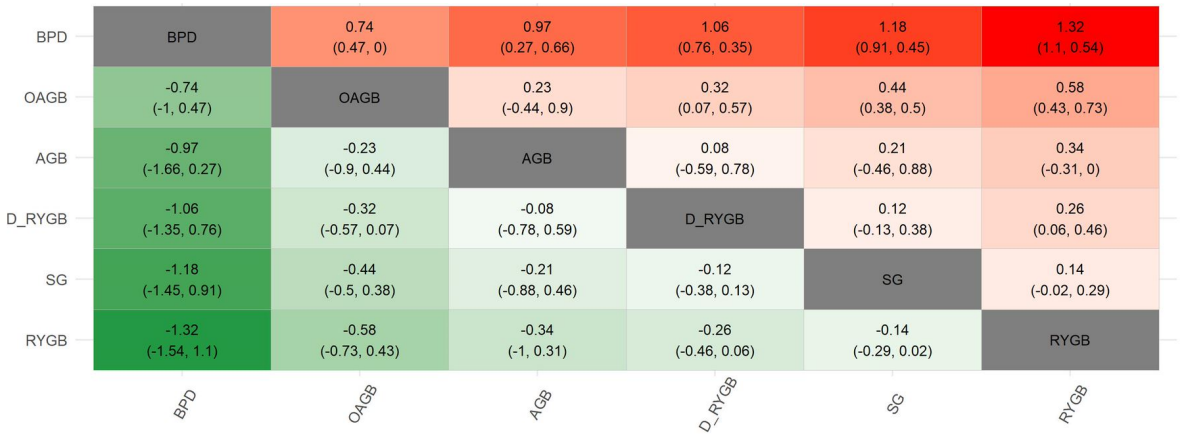

Figure A16: Heatmap SMD diabetes outcomes at 2 years follow-up (fixed effect)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: BPD: biliopancreatic diversion; D_RYGB: distal Roux-en-Y gastric bypass; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

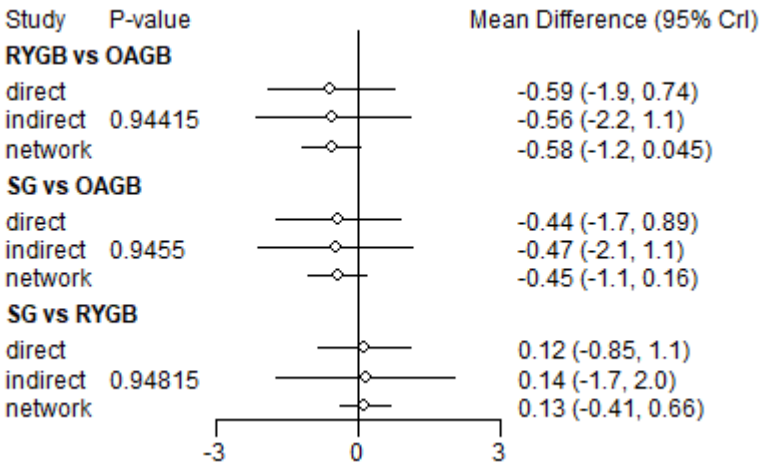

Figure A17: Nodesplit SMD diabetes outcomes at 2 years follow-up (fixed effect)

DIABETES 2 YEARS NMA RESULTS -RANDOM EFFECT

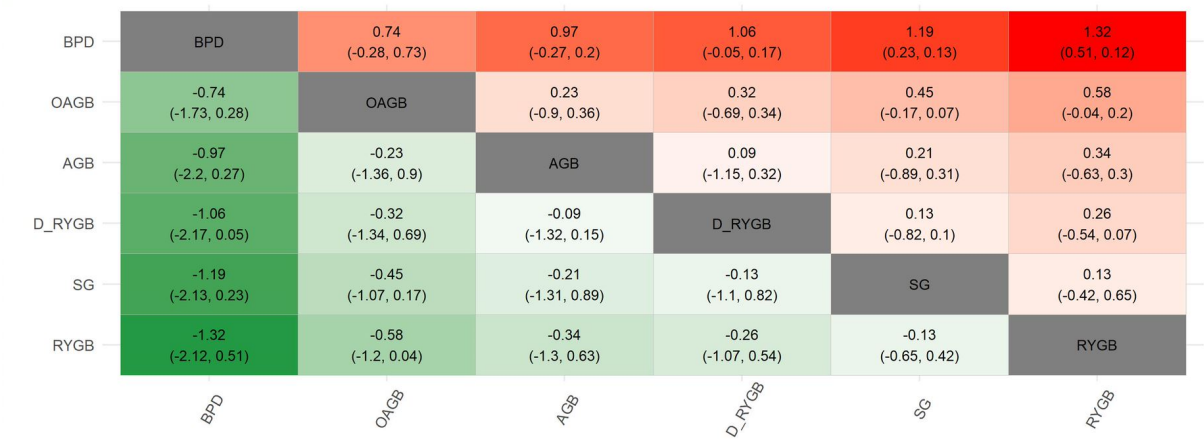

Figure A18: Heatmap SMD diabetes outcome at 2 years follow-up (random)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: BPD: biliopancreatic diversion; D_RYGB: distal Roux-en-Y gastric bypass; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

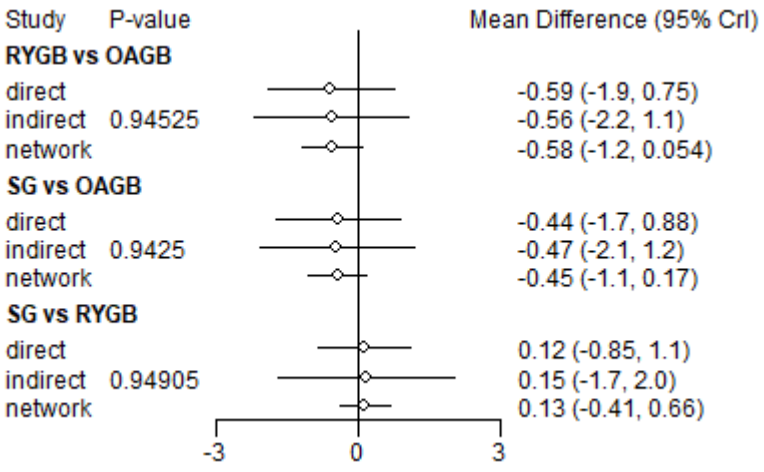

Figure A19: Nodesplit SMD diabetes outcome at 2 years follow-up (random)

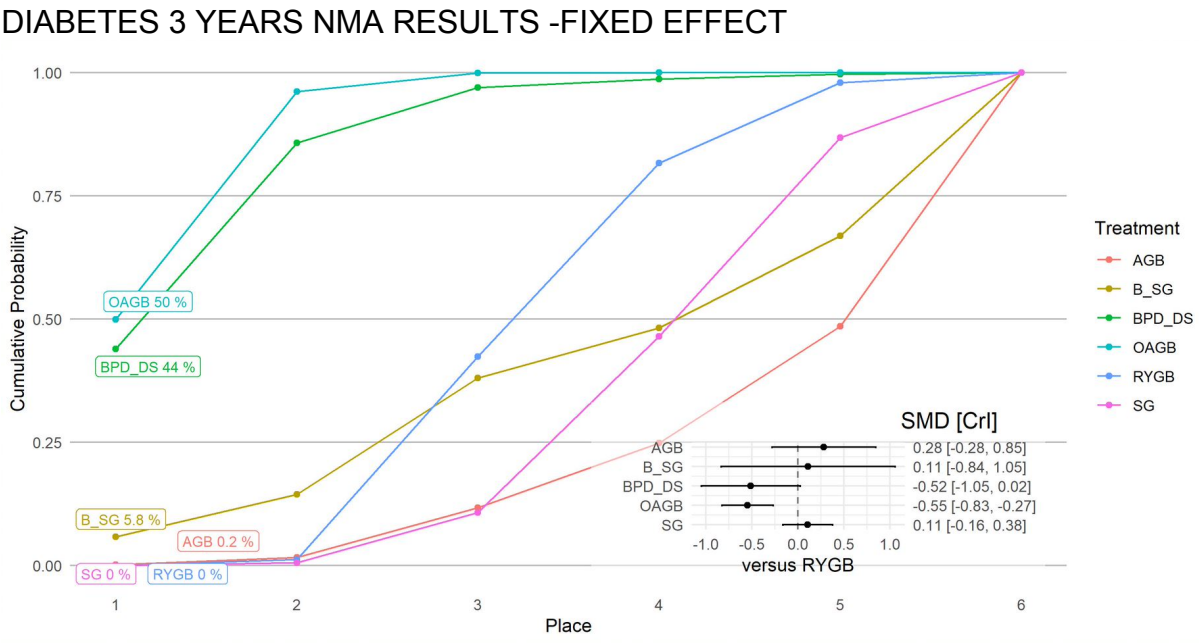

Figure A20: Sucra plot SMD diabetes outcomes at 3 years follow-up (fixed effect)

SUCRA (colored plot): Treatments are displayed according to their probability to achieve a specific rank (or better). In specific, OAGB has 49.9% probability to rank first and BPD-DS a 44.1% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual treatments might achieve a high ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is only judged to be relevant if the credibility intervals of the forest plots show superiority.

Abbreviations: B_SG: banded sleeve gastrectomy; BPD_DS: biliopancreatic diversion with duodenal switch; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

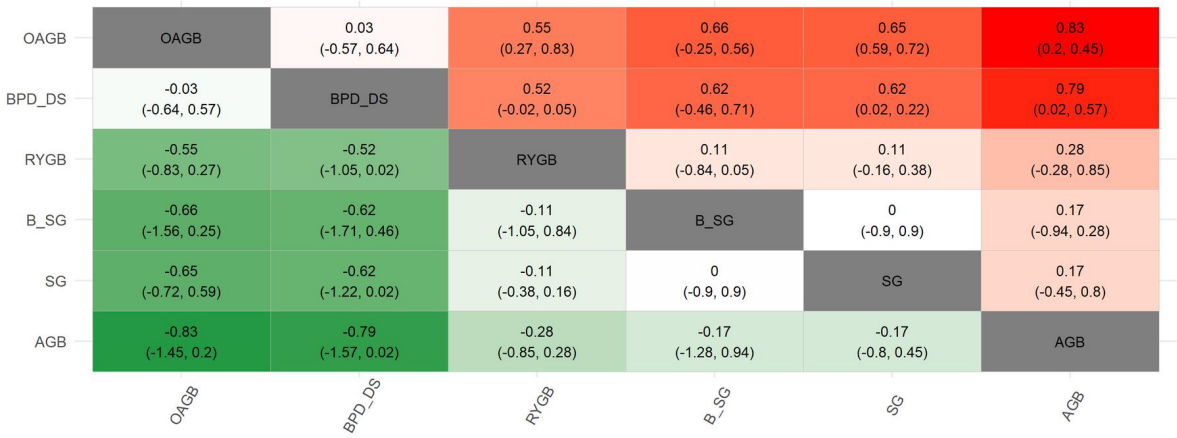

Figure A21: Heatmap SMD diabetes outcome at 3 years follow-up (fixed)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: B_SG: banded sleeve gastrectomy; BPD_DS: biliopancreatic diversion with duodenal switch; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

DIABETES 3 YEARS NMA RESULTS- RANDOM EFFECT

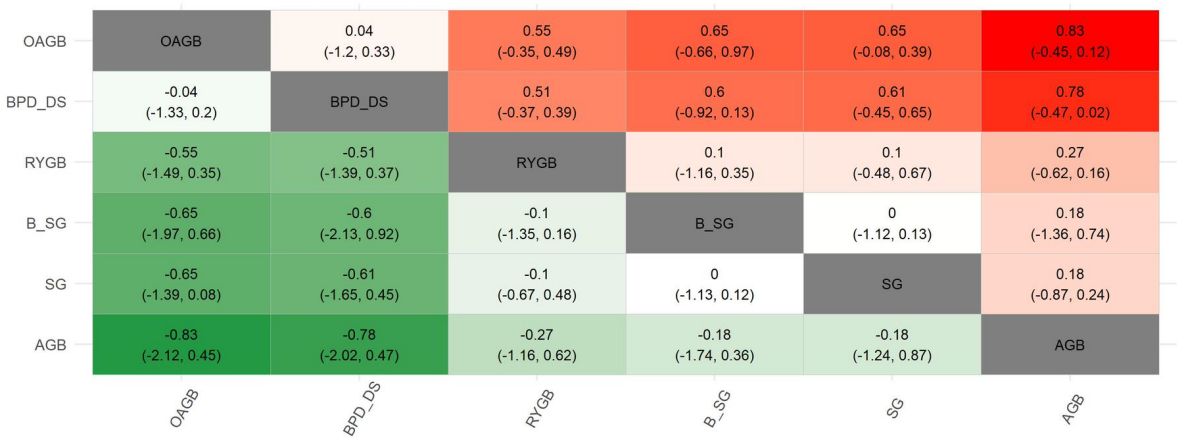

Figure A22: Heatmap SMD diabetes outcome at 3 years follow-up (random)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: B_SG: banded sleeve gastrectomy; BPD_DS: biliopancreatic diversion with duodenal switch; LAGB: laparoscopic adjustable gastric banding; OAGB: One anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

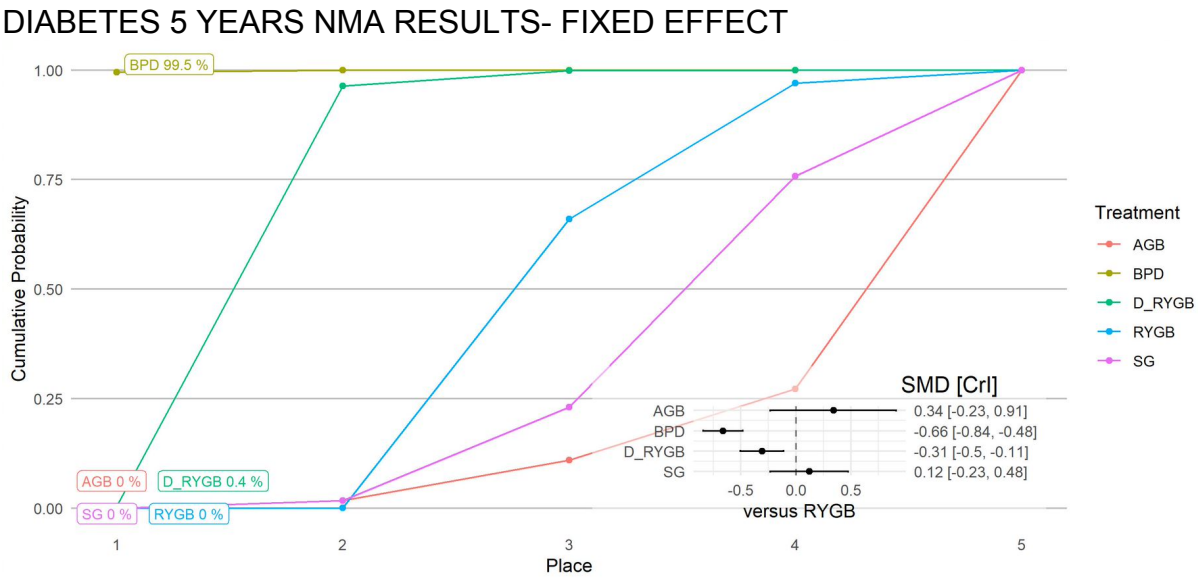

Figure A23: Sucra plot SMD diabetes outcomes at 5 years follow-up (fixed effect)

SUCRA (colored plot): Treatments are displayed according to their probability to achieve a specific rank (or better). In specific, BPD has 99.5% probability to rank first and D-RYGB a 0.5% probability to rank first. These rankings need to be set in relation to the effect sizes and credibility intervals since individual treatments might achieve a high ranking probability due to broad credibility intervals. Hence, we combined the SUCRA with forest plots. A good ranking is only judged to be relevant if the credibility intervals of the forest plots show superiority.

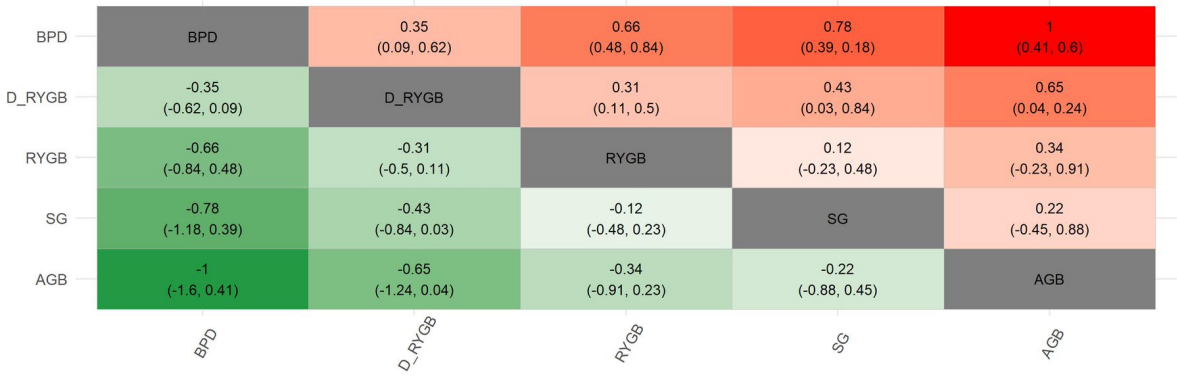

Figure A24: Heatmap SMD diabetes outcome at 5 years follow-up (fixed effect)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: BPD: biliopancreatic diversion; D_RYGB: distal Roux-en-Y gastric bypass; LAGB: laparoscopic adjustable gastric banding; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

DIABETES 5 YEARS NMA RESULTS- RANDOM EFFECT

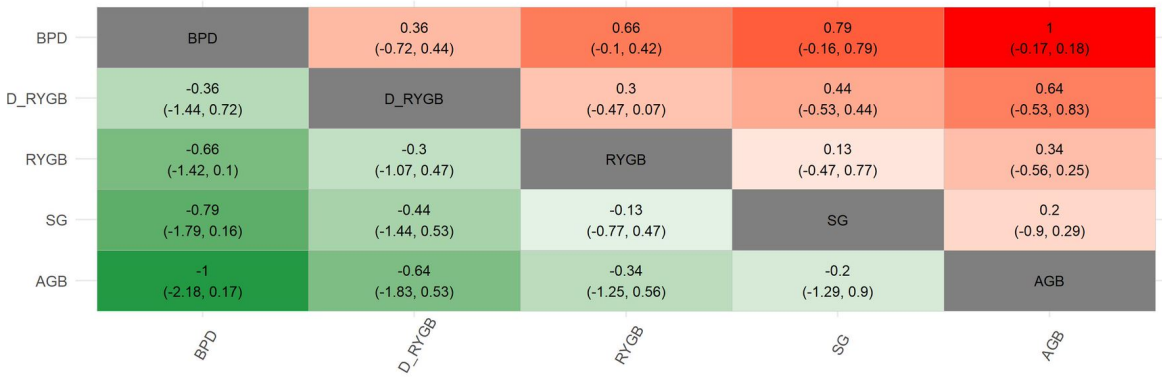

Figure A25: Heatmap SMD diabetes outcome at 5 years follow-up (random effect)

All treatments included in the network compared with each other. Figure is meant to be read from top to down and left to right. For instance, the first column shows the pooled effect sizes (and credibility intervals) of the treatment with the best effect sizes versus all others. Effect sizes are further colored according to the differences to their comparators (from green to red).

Abbreviations: BPD: biliopancreatic diversion; D_RYGB: distal Roux-en-Y gastric bypass; LAGB: laparoscopic adjustable gastric banding; RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy

Outcome measures used for the SMD calculations: weight-related outcomes and diabetes

Diabetes control outcomes used for the SMD calculations

1. Mean HbA1c (%)	2.HbA1c %	**3.** Mean change in HbA1c (%) from BL	**4.** Mean % change in HbA1c from BL	**5.** Mean change in HbA1c (mmol/mol) from BL	**6.** Fasting plasma glucose (FPG) (mg/dL) or (mmol/L)	**7.** Mean change in FPG from BL	**8.** Mean % change in FPG from BL
2 yrs follow up							
Courcoulas/TRIABETES, Mingrone/DIBASY; Robert/YOMEGA; Schauer/STAMPEDE; Seethamariah; Svanevik		Wallenius			-		
3 yrs follow up							
Courcou-		-			Salminen		

las/TRIABETES; Fink/MISO; Hedberg; Schau-er/STAMPEDE; Seethamariah							
5 yrs follow up							
Mingrone/DIBASY; Schauer/STAMPED E; Svanevik		-			Salminen		

Weight related outcomes used for the SMD calculations

1.BMI (kg/m2)	2. Mean% excess weight loss	3. Mean change in BMI from BL	4.Weight (kg)	5. Mean weight change (kg) from BL	6. Mean% weight change from BL
2 years follow up					
Angrisani, Arceo, Biter, Courcoulas, Fink, Ignat, Mingrone, Peterli, Ristad, Schauer, Zhang	Nguyen, Rasera, Seth-amariaha, Wallenius			Robert	
3 years follow up					
Angrisani, Courcou-las, Fink, Ignat, Keg-agias, Peterli, Salminen, Tognoni, Zhang	Hedberg, Himpens, Nguyen, Seeth-amariaha		Schauer		
5 years follow up					
Angrisani, Arceo - Olfaiz, Courcoulas Ignat, Mingrone, Pe-terli, Risstad, Salminen, Zhang		Svanevik	Schauer		
10 years follow-up					
Angrisani		Nguyen			
Not included in the analyses: 4 yrs follow up: Courcoulas, Ignat, Nguyen, Peterli, Tognoni, Zhang					

APPENDIX 6: EVIDENCE GAPS TABLE WITH GUIDANCE

Table A31: The author completes the table and sends it to WP5B

1. EVIDENCE PROFILE OF THE TECHNOLOGY				
Topic and rationale				
Title of the assessment	*[Title of the assessment]*			
Research question	*[Structured research question]*			
Rationale	*[Clear statement on rationale supporting the use of technology explaining how its intrinsic characteristics can lead to improvement on patient-important outcomes compared to current management, potential of the technology to cover unmet health care need (if applicable), and information on burden of disease]*			
PICO				
Population	*[Health status, disease, inclusion/exclusion criteria]*			
Intervention	*[Technology and setting of use]*			
Comparator(s)	*[Relevant comparator(s) and setting of use]*			
The most important/critical outcomes (based on discussions with clinical experts)	*[Name of the outcome, measurement tool and desired effect size]*			
	[Name of the outcome, measurement tool and desired effect size]			
	[Name of the outcome, measurement tool and desired effect size]			
	[Name of the outcome, measurement tool and desired effect size]			
	[Name of the outcome, measurement tool and desired effect size] *(Make copies of the lines above, if needed)*			
Study design(s)	*[Study design(s) which can produce robust and transferable results; may differ between outcomes]*			
2. ASSESSMENT RESULTS				
Most important/critical outcomes where evidence currently lacking or considered insufficient *[Please see Summary of findings table (if applicable)]*	**No. of studies**	**Type of studies**	**Estimate of effect size *[1]**	**Certainty of the evidence *[2]**
[Outcome 1]	*[No. of studies]*	*[Study design(s)]*	*[Estimate of effect size]*	*[Level of certainty]*
[Outcome 2]	*[No. of studies]*	*[Study design(s)]*	*[Estimate of effect size]*	*[Level of certainty]*

[Outcome 3]	*[No. of studies]*	*[Study design(s)]*	*[Estimate of effect size]*	*[Level of certainty]*
[Outcome 4]	*[No. of studies]*	*[Study design(s)]*	*[Estimate of effect size]*	*[Level of certainty]*
[Outcome 5]	*[No. of studies]*	*[Study design(s)]*	*[Estimate of effect size]*	*[Level of certainty]*

(Make copies of the lines above, if needed)

3. ADDITIONAL EVIDENCE GENERATION NEEDS	
Research question 1: *[Structured research question]*	
Evidence	*[Current state of the evidence available/reasons for uncertainty]*
Population	*[Population and any sub-population(s) of interest]*
Intervention	*[The technology/intervention and setting of use]*
Comparator	*[Relevant comparator and setting of use]*
Outcome(s)	*[Outcome(s) of interest]*
Time stamp	*[Date of recommendation]*
Study design	*[Appropriate study design]*
Ongoing studies	*[Study registry numbers of relevant ongoing studies, with the date when the search for ongoing studies was performed]* Please delete the row if no ongoing studies have been identified
Research question 2: *[Structured research question]*	
Evidence	*[Current state of the evidence available/reasons for uncertainty]*
Population	*[Population and any sub-population(s)of interest]*
Intervention	*[The technology/intervention and setting of use]*
Comparator	*[Relevant comparator and setting of use]*
Outcome(s)	*[Outcome(s) of interest]*
Time stamp	*[Date of recommendation]*
Study design	*[Appropriate study design]*
Ongoing studies	*[Study registry numbers of relevant ongoing studies, with the date when the search for ongoing studies was performed]* Please delete the row if no ongoing studies have been identified
Research question 3: *[Structured research question]* *(Make copies of the lines above, if needed)*	

*[1] If differences in results for different sub-populations, please adapt the table in order to allow reporting of these differences

*[2] If no evidence grading system is used, please provide a short narrative statement about the certainty of the evidence

Table A32: To be included as an appendix in the assessment report or as a separate document to the assessment report

ADDITIONAL EVIDENCE GENERATION NEEDS	
Research question 1: What is the relative effect of the different bariatric surgical procedures on mortality?	
Evidence	Based on the available information from this review it was not possible to say whether there may be an increased risk of early or late death with any, or all, of these procedures.
Population	Adult people with obesity, with or without comorbidities
Intervention	All interventions within the scope of this assessment
Comparator	As listed above
Outcome(s)	Mortality, cause of death
Time stamp	May 2021
Study design	RCT
Ongoing studies	Mortality is registered as an outcome for one ongoing study comparing RYGB with SG. Date of search June 2020
Research question 2: What is the relative effect of the different bariatric surgical procedures on weight loss?	
Evidence	Low to moderate certainty (depending on the length of follow-up) in the evidence, based on five trials that compared RYGB vs SG. Low certainty evidence for the comparisons RYGB vs AGB, RYGB vs OAGB, SG vs OAGB, SG vs AGB. There is no evidence for the effect on weight loss for the comparisons. For the other comparisons, there is either no evidence or evidence coming from a single study only.
Population	Adult people with obesity, with or without comorbidities
Intervention	All interventions within the scope of this assessment, the comparison RYGB vs SG is of a lower priority.
Comparator	As listed above
Outcome(s)	BMI, Mean% excess weight loss, Mean change in BMI from BL, Weight (kg), Mean weight change (kg) from BL, Mean% weight change from BL Long term follow-up periods (5, 10y) to be prioritized.
Time stamp	May 2021
Study design	RCT
Ongoing studies	Six ongoing trials have diabetes related outcomes registered for the comparison RYGB with SG, and one trial each for the comparisons RYGB vs OAGB RYGB vs SADI, RYGB vs AGB.
Research question 3: What is the relative effect of the different bariatric surgical procedures on diabetes control?	

Evidence	Low certainty evidence for RYGB vs SG, SG vs OAGB and very low certainty evidence for RYGB vs OAGB. For the other comparisons, there is either no evidence or evidence coming from a single study only.
Population	Adult people with obesity, with or without comorbidities
Intervention	All interventions within the scope of this assessment
Comparator	As listed above
Outcome(s)	Mean% change in FPG from BL, Mean change in FPG from BL, Fasting plasma glucose (FPG) (mg/dL) or (mmol/L), Mean change in HbA1c (mmol/mol) from BL, Mean% change in HbA1c from BL, Mean change in HbA1c (%) from BL, HbA1c%, Mean HbA1c (%). Long term follow-up periods (5, 10y) to be prioritized.
Time stamp	May 2021
Study design	RCT
Ongoing studies	Six ongoing trials have diabetes related outcomes registered for the comparison RYGB with SG, and one trial each for the comparisons RYGB vs OAGB RYGB vs SADI, RYGB vs AGB.

Research question 4: Do the bariatric surgical procedures differ in their effect on generic health related quality of life?	
Evidence	Low certainty evidence, based on 11 studies, that there is little or no differences in HRQOL between procedures for six comparisons (RYGB, SG, OAGB, BPD-DS, SR-RYGB, D-RYGB; B-SG). For the other comparisons, there is either no evidence or evidence coming from a single study only.
Population	Adult people with obesity, with or without comorbidities
Intervention	All interventions within the scope of this assessment
Comparator	As listed above
Outcome(s)	Health Related Quality of Life. Long term follow-up periods (5, 10y) to be prioritized.
Time stamp	May 2021
Study design	RCT
Ongoing studies	Four ongoing studies focus on quality of life outcomes for the comparison RYGB vs SG, one study comparing RYGB with vs AGB and one study with OAGB. Date of search June 2020.