

Region Västra Götaland, HTA-centrum

Regional activity-based HTA [Verksamhetsbaserad HTA]

Health Technology Assessment

HTA-report 2016:92

Bariatric surgery for diabetes mellitus type 2 control in adults with BMI<35 kg/m²

Fändriks L, Daxberg E-L, Eliasson B, Eriksson M, Jivegård L, Persson J, Sandqvist M, Wallenius V, Sjögren P

Bariatric surgery for diabetes mellitus type 2 control in adults with BMI<35 kg/m²

[Bariatrisk kirurgi som behandling av diabetes mellitus typ 2 hos vuxna med ett BMI<35 kg/m²]

Fändriks L^{1,2*}, Daxberg E-L³, Eliasson B⁴, Eriksson M³, Jivegård L⁵, Persson J⁵, Sandqvist M⁴, Wallenius V¹, Sjögren P⁵

¹ Department of Surgery, Sahlgrenska University Hospital, Göteborg, Sweden

² Department of Gastrosurgical Research and Education, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden

³ Medical Library, Sahlgrenska University Hospital, Göteborg, Sweden

⁴ Department of Medicine, Sahlgrenska University Hospital, Göteborg, Sweden

⁵ HTA-centrum, Region Västra Götaland, Sahlgrenska University Hospital, Gothenburg, Sweden

*Corresponding author

Published November 2016

2016:92

Suggested citation: Fändriks L, Daxberg E-L, Eliasson B, Eriksson M, Jivegård L, Persson J, Sandqvist M, Wallenius V, Sjögren P. Bariatric surgery for diabetes mellitus type 2 control in adults with BMI<35 kg/m² [Bariatrisk kirurgi som behandling av diabetes mellitus typ 2 hos vuxna med ett BMI<35 kg/m²]. Göteborg: Västra Götalandsregionen, Sahlgrenska Universitetssjukhuset, HTA-centrum; 2016. Regional activity-based HTA 2016:92

Table of contents

1. Abstract.....	4
2. Svensk sammanfattning – Swedish summary	4
3. Summary of Findings (SoF-table)	7
4. Abbreviations.....	9
5. Background.....	10
6. Health Technology	12
7. Objective.....	13
8. Methods	14
9. Results	15
10. Ethical consequences.....	18
11. Organisation.....	18
12. Economy aspects	20
13. Discussion.....	21
14. Future perspective.....	22
15. Participants in the project.	23

Appendix 1 Search strategy, study selection and references

Appendix 2 Included studies – design and patient characteristics

Appendix 3 Excluded articles

Appendix 4 Outcome tables

1. Abstract

Background: Obesity is strongly linked to diabetes and premature mortality, mainly from cardiovascular causes. In 2013, the prevalence of obesity (BMI ≥ 30 kg/m²) in adults in Sweden was 14 %. The prevalence of diabetes mellitus in Sweden is approximately 5 % with a slow increase due to an ageing population. In 2015, 73,225 patients in VGR had a diagnosis of diabetes mellitus.

The treatment of overweight and obesity in adults is based on three principles: lifestyle changes, pharmacological treatment and surgery. Today, weight reducing (bariatric) surgery can be offered to individuals with BMI ≥ 40 kg/m², and patients with BMI ≥ 35 kg/m² with an obesity associated disease, in particular diabetes mellitus type 2 (T2D). Bariatric surgery in persons with BMI < 35 kg/m² is currently not endorsed in Swedish national guidelines (National Board of Health and Welfare, 2015). Glycaemic stabilisation is reported to occur very early after surgery, before any significant weight loss. In a recent joint statement by several international diabetes organizations, it was proposed that bariatric surgery should be considered to be an option to treat T2D in patients with BMI 30.0–34.99 kg/m² and inadequately controlled hyperglycaemia despite optimal medical treatment.

Objective: To study if bariatric surgery in patients with T2D and a BMI < 35 kg/m² is superior to standard treatment with regard to diabetes control.

Search methods and study selection criteria: During January 2016 two authors performed systematic searches in PubMed, Embase, the Cochrane Library and a number of HTA-databases for systematic reviews, randomized (RCT) and non-randomised controlled studies. Due to the small number of original articles fulfilling the inclusion criteria we chose to only include and critically appraise original articles.

Main results: The literature search resulted in four RCTs and six cohort studies (two reporting on the same population) comparing results of bariatric surgery with medical treatment in T2D patients with BMI < 35 kg/m². The studies had limitations mainly related to, e.g., short follow-up, some inconsistency, indirectness due to different interventions or unclear patient selection, and imprecision. Mortality was reported in two studies with only one reported death. Remission of T2D was studied in three RCTs and four cohort studies. The frequency of T2D remission during 1–3 years follow-up may be higher after bariatric surgery compared with non-surgical standard care (GRADE $\oplus\oplus\circ\circ$). Diabetes related and cardiovascular complications were not studied. Health related quality of life (SF-36) was reported in one RCT and physical wellbeing may improve after bariatric surgery compared with medical treatment (GRADE $\oplus\oplus\circ\circ$). Regarding glycaemic control, bariatric surgery compared with non-surgical standard care probably reduces HbA_{1c} (GRADE $\oplus\oplus\oplus\circ$), may reduce fasting plasma glucose (GRADE $\oplus\oplus\circ\circ$) but the effect on the number of glucose-lowering medications is uncertain (GRADE $\oplus\circ\circ\circ$). Bariatric surgery compared with non-surgical standard care probably reduces BMI (GRADE $\oplus\oplus\oplus\circ$) but the effects on other metabolic risk factors are uncertain (GRADE $\oplus\circ\circ\circ$).

Risks and complications: The rate of surgical complications was reported from four to 17% ranging from mild to more severe complications requiring surgical intervention.

Concluding remarks: This systematic review shows that bariatric surgery compared with medical treatment may increase the frequency of diabetes remission and probably results in improved glycaemic control in adults with overweight or obesity (BMI < 35 kg/m², mainly 30 – 34.99 kg/m²) during 1–3 years follow-up. The bariatric surgical procedures mainly performed in Sweden today (Roux-en-Y gastric bypass, vertical sleeve gastrectomy) were investigated in only half of the current studies. Data on long term efficacy and safety are lacking and there are no results indicating reduced risk of cardiovascular disease, cancer or death. No relevant health economic analyses are available.

2. Svensk sammanfattning – Swedish summary

Bakgrund: Fetma är starkt kopplad till diabetes och för tidig död, framför allt av kardiovaskulära orsaker. År 2013 var prevalensen av fetma ($\text{BMI} \geq 30 \text{ kg/m}^2$) hos vuxna i Sverige 14 %. Prevalensen av diabetes mellitus i Sverige är cirka 5 % med långsam ökning till följd av åldrande befolkning. I Västra Götalandsregionen år 2015 hade 73 225 patienter diagnosen diabetes mellitus.

Behandling av övervikt och fetma hos vuxna bygger på tre principer; livsstilsförändringar, läkemedelsbehandling och kirurgi. Idag kan viktreducerande (bariatrisk) kirurgi erbjudas till individer med $\text{BMI} \geq 40 \text{ kg/m}^2$, samt individer med $\text{BMI} \geq 35 \text{ kg/m}^2$ som har fetmarelaterad sjukdom, i synnerhet typ 2-diabetes (T2D). Bariatrisk kirurgi för individer med $\text{BMI} < 35 \text{ kg/m}^2$ rekommenderas inte idag i de svenska nationella riktlinjerna (Socialstyrelsen, 2015). Förbättrad diabeteskontroll har noterats väldigt tidigt efter kirurgi, före signifikant viktminskning. I ett gemensamt uttalande från flera internationella diabetesorganisationer föreslogs nyligen att bariatrisk kirurgi bör ses som ett alternativ för behandling av T2D hos patienter med $\text{BMI} 30,0\text{-}34,99 \text{ kg/m}^2$ och bristfälligt kontrollerat sockerläge trots optimal medicinsk behandling.

Syfte: Att studera huruvida bariatrisk kirurgi jämfört med standardbehandling hos patienter med T2D och $\text{BMI} < 35 \text{ kg/m}^2$ ger bättre diabeteskontroll.

Metod: Under januari 2016, utförde två av författarna systematiska litteratursökningar i PubMed, Embase, Cochrane Library och ett antal HTA-databaser, för att identifiera systematiska översikter, randomiserade- (RCT) och icke-randomiserade kontrollerade studier. På grund av det begränsade antalet originalartiklar som uppfyllde inklusionskriterierna beslutades att endast originalartiklar skulle inkluderas och granskas.

Resultat: Litteratursökningen resulterade i fyra RCT och sex kohortstudier (två rapporterade från samma material) som jämförde bariatrisk kirurgi med medicinsk behandling av T2D patienter med $\text{BMI} < 35 \text{ kg/m}^2$. Studierna hade brister i huvudsak relaterade till korta uppföljningstider, överförbarhet (olika interventioner), oklarheter i patienturval och bristande precision. Mortalitet rapporterades i två studier med endast ett rapporterat dödsfall. Remission av T2D studerades i tre RCT och fyra kohortstudier, och frekvensen av remission av T2D under 1-3 års uppföljning kan vara högre efter bariatrisk kirurgi jämfört med icke-kirurgisk standardbehandling (GRADE ⊕⊕○○). Diabetesrelaterade komplikationer eller kardiovaskulära komplikationer var inte studerade. Hälsorelaterad livskvalitet (SF-36) rapporterades i en RCT, och fysisk välbefinnande kan förbättras efter bariatrisk kirurgi jämfört med medicinsk behandling (GRADE ⊕⊕○○). Avseende glykemisk kontroll sänker troligen bariatrisk kirurgi jämfört med icke-kirurgisk standardbehandling HbA1c (GRADE ⊕⊕⊕○), kan sänka fasteblodsocker (GRADE ⊕⊕○○), medan det är osäkert huruvida antalet glukossänkande läkemedel påverkas (GRADE ⊕○○○). Bariatrisk kirurgi sänker troligen BMI jämfört med standardbehandling (GRADE ⊕⊕⊕○), medan effekterna på övriga metabola riskfaktorer är osäkra (GRADE ⊕○○○).

Risker och komplikationer: Förekomsten av kirurgiska komplikationer varierade från fyra till 17 %, med alltifrån lindriga till mer allvarliga komplikationer som krävde kirurgisk behandling.

Sammanfattande kommentar: Denna systematiska översikt visar att bariatrisk kirurgi jämfört med medicinsk behandling kan öka remissionsfrekvensen av diabetes mellitus typ 2 och troligen resulterar i en förbättrad glykemisk kontroll hos överviktiga och obesa patienter med $\text{BMI} < 35 \text{ kg/m}^2$ (främst $30 - 34,99 \text{ kg/m}^2$) under 1-3 års uppföljning. De i Sverige idag huvudsakligen använda ingreppen inom bariatrisk kirurgi (Roux-en-Y gastric bypass, vertikal sleeve gastrectomy) studerades i endast hälften av de inkluderade studierna. Kunskap om långsiktig patientnytta och säkerhet saknas och det finns idag inga resultat som indikerar minskad risk för kardiovaskulära sjukdomar, cancer eller dödlighet. Inga relevanta hälsoekonomiska analyser kunde identifieras.

The above summaries were written by representatives from the HTA-centrum. The HTA-report was approved by the Regional board for quality assurance of activity-based HTA. The abstract is a concise summary of the results of the systematic review. The Swedish summary is a brief summary of the systematic review intended for decision makers, and is ended with a concluding summary.

Christina Bergh, Professor, MD

Head of HTA-centrum of Region Västra Götaland, Sweden, 2016-10-26

Christina Bergh

MD, Professor

Elisabeth Hansson-Olofsson

PhD, Senior lecturer

Magnus Hakeberg

OD, Professor

Lennart Jivegård

MD, Senior university lecturer

Jenny Kindblom

MD, Associate professor

Anders Larsson

MD, PhD

Olle Nelzén

MD, Associate professor

Christian Rylander

MD, PhD

Ola Samuelsson

MD, Associate professor

Ninni Sernert

Associate professor

Henrik Sjövall

MD, Professor

Petteri Sjögren

DDS, PhD

Maria Skogby

RN, PhD

Annika Strandell

MD, Associate professor

Therese Svanberg

HTA-librarian

3. Summary of Findings

Table 1. Main findings in controlled studies on bariatric surgery for type 2 diabetes mellitus control in adults with BMI<35 kg/m² (Appendix 4)

Outcomes	Study design and number	Relative effect (95% CI)	Absolute effect	Certainty of evidence GRADE*																																
Critical for decision-making																																				
Mortality	1 RCT 1 Cohort	Not calculated	One fatal heart event in control group	⊕○○○ Very low ¹																																
Remission of type-2 diabetes	3 RCT 4 Cohort	Not calculated	<table border="1"> <thead> <tr> <th>Design</th> <th>Surgery</th> <th>No surgery</th> <th>p-value</th> </tr> </thead> <tbody> <tr> <td>RCT</td> <td>28/31</td> <td>0/36 0/34</td> <td><0.0001[†]</td> </tr> <tr> <td>RCT</td> <td>0/12</td> <td>0/11</td> <td>n.s. [†]</td> </tr> <tr> <td>RCT</td> <td>12/25</td> <td>2/26</td> <td>0.001[†]</td> </tr> <tr> <td>Cohort</td> <td>8/9</td> <td>0/9</td> <td>0.0004[†]</td> </tr> <tr> <td>Cohort</td> <td>5/20</td> <td>0/27</td> <td><0.0001[†]</td> </tr> <tr> <td>Cohort</td> <td>9/30</td> <td>0/38</td> <td>0.0003[†]</td> </tr> <tr> <td>Cohort</td> <td>11/17</td> <td>not stated</td> <td>not stated</td> </tr> </tbody> </table>	Design	Surgery	No surgery	p-value	RCT	28/31	0/36 0/34	<0.0001 [†]	RCT	0/12	0/11	n.s. [†]	RCT	12/25	2/26	0.001 [†]	Cohort	8/9	0/9	0.0004 [†]	Cohort	5/20	0/27	<0.0001 [†]	Cohort	9/30	0/38	0.0003 [†]	Cohort	11/17	not stated	not stated	⊕⊕○○ Low ¹
Design	Surgery	No surgery	p-value																																	
RCT	28/31	0/36 0/34	<0.0001 [†]																																	
RCT	0/12	0/11	n.s. [†]																																	
RCT	12/25	2/26	0.001 [†]																																	
Cohort	8/9	0/9	0.0004 [†]																																	
Cohort	5/20	0/27	<0.0001 [†]																																	
Cohort	9/30	0/38	0.0003 [†]																																	
Cohort	11/17	not stated	not stated																																	
Diabetes related complications: The outcome was not studied																																				
Cardiovascular complications: The outcome was not studied																																				
Health related quality of life (HRQoL)	1 RCT	Not calculated	<p><u>SF-36, Physical wellbeing (mean, 95% CI)</u> Surgery No surgery 7.7 (5.0 to 10.4) -1.7 (-5.3 to 1.9), p<0.0001</p> <p><u>SF-36, Mental wellbeing (mean, 95% CI)</u> Surgery No surgery -0.13 (-6.8 to 6.5) -0.82 (-5.2 to 3.6), n.s.</p>	⊕⊕○○ Low ¹																																
Important for decision-making																																				
Glycaemic control (HbA1c)	4 RCT 5 Cohort	Not calculated	<p>4 RCT, HbA1c mean changes, range (% units): Surgery groups: -0.8 to -4.5 No surgery groups: 0.1 to -3.42</p> <p>4 RCT: p=0.0013 (favours surgery) to n.s. 5 Cohort: p<0.05 to n.s (not stated in 2)</p>	⊕⊕⊕○ Moderate ¹																																
Less important for decision-making																																				
Other metabolic risk factors (i.e. dyslipidaemia, hypertension, sleep apnoea)	2 RCT 6 Cohort	Not calculated	Uncertain effects on dyslipidaemia, hypertension, sleep apnoea in the surgery compared with the control groups	⊕○○○ Very low ¹																																
Body Mass Index (BMI) or body weight	4 RCT 6 Cohort	Not calculated	<p>4 RCT, range of mean changes in BMI: Surgery groups: from -7% to -20% No surgery groups: from -0.5% to -2%</p> <p>4 RCT: p<0.0001 to <0.05 (favours surgery) 2 Cohort: p<0.001 to < 0.05 (favours surgery) 4 Cohort: p-values not stated</p>	⊕⊕⊕○ Moderate ¹																																

Table 1 contd. Main findings in controlled studies on bariatric surgery for type 2 diabetes mellitus control in adults with BMI<35 kg/m² (Appendix 4)

Fasting plasma glucose (FPG)	2 RCT 4 Cohort	Not calculated	1 RCT, intergroup difference (SD) mmol/l: 1.9 (0.6 to 3.1) p=0.0038 (favours surgery) 1 RCT: mean difference (SD) mg/dl: surgery: -57 p=0.0038, no surgery -41, n.s. 3 cohort, range of mean changes in FPG surgery groups:-100 to -52 mg/dl no surgery groups: -29 to 15 mg/dl p-values from n.s. to <0.05 (favours surgery) 1 cohort, mean change, Surgery group: -1.6 mmol/l No surgery group: -0.6 mmol/l, p <0.05 (favours surgery)	⊕⊕○○ Low ¹
Use of glucose lowering medication	2 RCT 2 Cohort	Not calculated	1 RCT, medication score mean change, surgery: -0.2, no surgery: +0.6. 1 RCT, mean number diabetes medications, surgery: ≈1.1, no surgery: ≈2.7 1 cohort, patients in need of diabetes medication, surgery: 37%, no surgery: 100% 1 cohort, medication scores, surgery: 14, no surgery: 9	⊕○○○ Very low ¹

Footnotes: [†] p-values calculated from presented data (Fisher's Exact test). ¹ Across the studied outcomes the RCTs had study limitations mainly related to short follow-up periods, inconsistencies between the individual study results, indirectness due to different interventions, unclear selection of patients, and imprecision due to few included patients. The cohort studies had limitations related to unclear selection of study groups, sometimes not adjusted for confounders, and indirectness due to different interventions across the studies.

*** Certainty of evidence**

High certainty ⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty ⊕⊕⊕○	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty ⊕⊕○○	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty ⊕○○○	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

4. Abbreviations/Acronyms

AGB	Adjustable gastric band
BMI	Body mass index
BPD	Biliary-pancreatic diversion
DJB	Duodeno-jejunal bypass
FPG	Fasting plasma glucose-concentration
HRQOL	Health related quality of life
HTA	Health technology assessment
IDF	International Diabetes Federation
RCT	Randomized controlled trial
RYGB	Roux-en-Y gastric bypass
SG	Sleeve gastrectomy
T2D	Type 2 diabetes mellitus
WHO	World Health Organisation

5. Background

Disease/disorder of interest and its degree of severity

Obesity is a rapidly escalating health concern, currently affecting more than 600 million adults worldwide according to the World Health Organisation, WHO (WHO 2016).

Obesity is strongly linked to type 2 diabetes mellitus (T2D), hypertension and blood lipid abnormalities, as well as to premature mortality, mainly from cardiovascular causes. The strong association between obesity and T2D is of particular significance; the increasing prevalence of obesity is associated with an epidemic of T2D, affecting 382 million of the worldwide adult population in 2013, with an expected increase to 587 million by 2035.

Prevalence of obesity and T2D in Sweden

The prevalence of obesity (BMI ≥ 30 kg/m²) in adults in Sweden in 2013 is 14 %. There has been a slow increase in prevalence from 11 % in the year 2004. The prevalence of overweight (BMI 25-29.9 kg/m²) is 42% in men and 29% in women (in 2013). The prevalence of T2D is probably around 5% with only a slow increase due to an ageing population (Jansson *et al.*, 2007). The incidence rate in Sweden is considered relatively stable. Incidence and prevalence rates of overweight, obesity and T2D is dramatically higher in many other countries (IDF Diabetes Atlas, IDF, 2015). There is a strong correlation between increasingly higher BMI and the incidence of type 2 diabetes (Ganz *et al.*, 2014). According to The Swedish National Diabetes Register (NDR, 2016) the annual prevalence was approximately 4,300 patients with T2D with a BMI of 30-35 kg/m² in Region Västra Götaland during 2012 to 2015.

Present treatment of overweight and obesity

The treatment of overweight and obesity in adults has been described in detail in two previous HTA-reports (Lönroth *et al.*, 2008; Eliasson *et al.*, 2015) In summary, such treatment is based on three general principles: lifestyle changes, pharmacology and surgery. Diet changes and caloric restriction, physical activity, behavioural therapy and use of pharmacologic treatments (currently only orlistat) are effective for providing weight loss, whereas the long term maintenance of the reduced body weight in most individuals is unsuccessful. According to present guidelines weight reducing (bariatric) surgery can be offered to persons with BMI ≥ 40 kg/m², and patients with BMI ≥ 35 kg/m² with an obesity associated disease, in particular T2D. Bariatric surgery is a surgical intervention of the gastrointestinal anatomy leading to an altered exposition of ingested nutrients to digestive factors. As of today two procedures dominate in bariatric surgery: the Roux-en-Y gastric bypass (RYGB) and the vertical sleeve gastrectomy (SG). Both procedures result (in most patients) in a large weight loss that is sustained over long time (Sjöström, 2013; Himpens *et al.*, 2010; Aminian *et al.*, 2016).

The choice of diabetes therapies is guided by national and regional treatment recommendations. Type 1 diabetes mellitus is treated with multiple daily insulin injections or continuous subcutaneous insulin infusion (insulin pump). Type 2 diabetes mellitus, which is strongly associated with obesity, can be treated with lifestyle changes (diet changes and physical activity) and eight different classes of pharmacological agents (Inzucchi *et al.*, 2015, National Board of Health and Welfare, 2015). Obese patients with BMI > 35 kg/m² and T2D can be offered bariatric surgery.

The normal pathway through the health care system and current wait time for medical assessment /treatment

Persons with overweight or obesity as well as individuals with T2D are generally treated in primary care. Persons with significant comorbidities or unstable or unsatisfactory glycaemic control can be referred to specialist clinics. There are currently no major problems with waiting time.

Number of patients per year who undergo current treatment regimen

The number of patients with BMI ≥ 35 kg/m² undergoing bariatric surgery is currently around 700 per year in Region Västra Götaland. Individuals with BMI <35 kg/m² are currently not offered bariatric surgery in public health care. The number of patients with T2D in Region Västra Götaland reported to the National Diabetes Register, and thus, undergoing any blood glucose-lowering treatment (diet, lifestyle or pharmacologic), was 73,225 in the year 2015.

Present recommendations from medical societies or health authorities

Bariatric surgery in persons with BMI < 35 kg/m² is currently not endorsed in Swedish national guidelines (National Board of Health and Welfare, 2015).

In a recent joint statement by several international diabetes organizations (but not including the Swedish, or the European Association for the Study of Diabetes, EASD), it was proposed that bariatric surgery “should also be considered to be an option to treat T2D in patients with class I obesity” (i.e. BMI 30.0–34.9 kg/m², reduced to 27.5 - 32.4 kg/m² for Asian patients) and for patients with “inadequately controlled hyperglycaemia despite optimal medical treatment by either oral or injectable medications (including insulin)” (National Board of Health and Welfare, 2015).

6. Bariatric surgery for type 2 diabetes mellitus control in adults with BMI < 35 kg/m²

During the 1970's, soon after bariatric surgery had become established as a treatment option for obesity, the National Institutes of Health, USA (NIH) started a series of consensus conferences for continuous scrutiny of the therapeutic results. An important consensus statement was published in 1991 describing the criteria for selection of patients eligible for obesity surgery (NIH, 1991). Selection criteria were mainly based on the proportional relationship between morbidity/mortality and the degree of overweight/obesity (BMI). The consensus statement concludes that obese patients with co-morbidity/-ies (e.g. cardiopulmonary problems and severe T2D) with a BMI ≥ 35 kg/m² could be offered surgical treatment. Based on the same association, BMI ≥ 40 kg/m² was considered sufficient for considering surgical treatment also in absence of comorbidities. BMI as primary selection criterion for surgical treatment was soon regarded as an oversimplification, and particularly the cut off-value at BMI 35 kg/m² for patients with co-morbidity was intensely debated. Although seriously questioned, these criteria still prevail in the current guidelines for bariatric surgery in most countries.

Another milestone paper with the provocative title "Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus" was published by Pories and collaborators in 1995 (Pories *et al.*, 1995). In this retrospective study data were presented suggesting that gastric bypass was associated with long-lasting improved glycemic control. However, adequately controlled trials were not available until the late 2000s showing improved diabetes control by obesity surgery, particularly so if performed early after onset. In addition, recent data from the Swedish Obese Subjects-study indicated that bariatric surgery prevents or at least delays onset of T2D in individuals with pre-diabetes (Carlsson *et al.*, 2012). Moreover, the metabolic improvements, particularly glycemic stabilization and blood pressure reduction, occur very early after surgery, before any significant weight-loss, indicating a direct effect on metabolic control by the gastrointestinal intervention. It follows that the reason for restricting surgical treatment of diabetics to patients with BMI ≥ 35 kg/m² was again challenged. The term 'metabolic surgery' was established to emphasise that the primary purpose of the procedure is not weight reduction *per se*, but rather the metabolic improvements, particularly the resolution of T2D, following surgery.

Very recently, a joint statement by representatives from several international organisations was presented, concluding that metabolic surgery should be considered as an option from a BMI of 30 kg/m² and above (Rubino *et al.*, 2016). This statement was based on data from several studies including T2D patients with BMI of 30 kg/m² and above. The results for patients with BMI 30–34.99 kg/m² were not presented separately, and the data do not support using a cut-off at BMI 35 kg/m². There are no technical problems associated with surgery for patients in the lower BMI interval, but the efficacy regarding T2D remission has been questioned. In addition, concerns have been raised regarding possible displacement effects within the health care system of the Region Västra Götaland (VGR) if patients in the lower BMI interval are offered bariatric surgery. The present HTA was undertaken to evaluate the scientific support for a clinical effect on T2D following bariatric surgery in patients with BMI below 35 kg/m².

7. Objective

The focused question

Is bariatric surgery in patients with type 2 diabetes mellitus and a BMI <35 kg/m² superior to standard treatment with regard to diabetes control?

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

P: Adult patients with type 2 diabetes mellitus (T2D) and BMI <35 kg/m²

I: Bariatric surgery (e.g. Roux-en-Y Gastric Bypass, Vertical Sleeve Gastrectomy) + non-surgical standard care (e.g. life style changes and pharmaceuticals)

C: Non-surgical standard care (e.g. life style changes and pharmaceuticals)

O: Critical for decision-making

Mortality

Remission from T2D

Diabetes related complications

Cardiovascular complications

Health related quality of life

Important for decision-making

Glycaemic control (HbA1c)

Less important for decision making

Other risk factors (dyslipidaemia, hypertension, sleep apnoea)

BMI, body weight, waist circumference

Fasting plasma glucose

Use of glucose lowering medication

Complications and risks

8. Methods

Systematic literature search (Appendix 1)

During January 2016 two authors (ME, ELD) performed systematic searches in PubMed, Embase, the Cochrane Library and a number of HTA-databases. Reference lists of relevant articles were also scrutinized for additional references.

At least two authors assessed the obtained abstracts, deciding which articles to read in full text. All participants of the project group read the articles independently of one another and it was finally decided in a consensus meeting which articles should be included in the assessment. Search strategies, eligibility criteria and a graphic presentation of the selection process are presented in Appendix 1.

Critical appraisal and certainty of evidence

The included studies, their design and patient characteristics are presented in Appendix 2. The excluded studies and the reasons for exclusion are listed in Appendix 3. The included studies were critically appraised using checklists from SBU (Swedish Agency for Health Technology Assessment and Assessment of Social Services) modified by HTA-centrum Västra Götaland for assessment of randomised (RCT) and non-randomised controlled trials respectively. The results and the assessed quality of each article were tabulated per outcome in Appendix 4. A summary-of-findings and the associated certainty of evidence for each outcome is presented in Table 1 (page 7). The certainty of evidence was defined according to the GRADE system (Atkins *et al.*, 2004; GRADE Working group). Grading the quality of evidence started at GRADE ⊕⊕⊕⊕ for the randomised and at ⊕⊕○○ for the non-randomised controlled studies.

Due to a relatively limited number of articles fulfilling the inclusion criteria we chose to only appraise original articles.

Ongoing research

A search in Clinicaltrials.gov 2016-05-09 using the search string ((Bariatric surger* OR Bariatric operation* OR Bariatric surgical procedure* OR Bariatric procedure* OR Biliopancreatic diversion OR Bilio-pancreatic diversion OR Biliopancreatic bypass OR Duodenojejunal bypass OR Duodenal jejunal bypass OR Duodenal switch OR Gastric bypass OR Gastroplast* OR Gastric band* OR Gastric sleeve* OR Gastric surgery OR Gastroenterostom* OR Gastrojejunostom* OR Ileal interposition OR Jejunioileal bypass OR Lap-band* OR Metabolic surger* OR Obesity surgery OR Roux-en-Y gastric bypass OR Roux-en Y OR Sleeve gastrectomy) AND (Diabet* OR T2DM OR Diabetes Mellitus, Type 2) AND (Body mass index OR BMI)) identified 76 trials.

9. Results

Systematic literature search (Appendix 1)

The literature search identified a total of 2,375 articles after removal of duplicates. It was then decided to only search for primary studies published after systematic reviews with final date of literature searches in 2014. In addition, primary publications included in those systematic reviews were also scrutinised for inclusion, resulting in a total of 692 records screened. Ninety-five of these records were read in full text, and another 68 articles were excluded (Appendix 3). The remaining 27 articles were read by all authors, of which 10 articles (four RCTs and six cohort studies) were finally included in the report (Appendix 2).

Results per outcome

Across the studies the four included RCTs had study limitations mainly related to short follow-up periods, inconsistencies between the individual study results, indirectness due to different interventions across the studies or unclear selection of patients, and imprecision due to few patients. The six included cohort studies, two of which reported on the same patient material, had limitations related to unclear selection of study groups, sometimes not adjusted for confounders, and indirectness due to different interventions across the studies.

Outcomes critical for decision making

Mortality (Appendix 4:1)

The included studies were underpowered for mortality as an outcome, thus lowering the precision. Mortality was reported in two studies: one RCT with one year follow up and one cohort study with two years follow up. The total number of patients was 176. One fatal myocardial infarction (MI) in the control group was reported (Scopinaro *et al.*, 2011a).

Conclusion: It is uncertain whether there is any difference in mortality after bariatric surgery compared with medical treatment in patients with T2D and a BMI <35 kg/m².

Very low certainty of evidence (GRADE ⊕○○○).

Remission of type 2 diabetes mellitus (Appendix 4:2)

Remission of T2D as outcome was reported in three RCTs and four cohort studies. Follow-up periods in the RCTs were 1-3 years (n=182). Surgical treatments included RYGB, gastric banding or duodenal-jejunal bypass surgery with minimal gastric resection, while the control groups were treated with standard or multidisciplinary care. Follow-up periods in the cohort studies were 1-3 years (n=167). Surgery included RYGB, sleeve gastrectomy or biliopancreatic diversion, and the control groups received standard medical care. In the three RCTs remission of T2D occurred in 0-90% in surgery groups and 0-8 % in the control groups (p value not reported in two of the studies, and p=0.0012 in Wentworth *et al.*, 2014). In the cohort studies the frequency of T2D remission was 25-89% in the surgery groups and 0% in the control groups (p-values not reported).

Conclusion: Bariatric surgery compared with medical therapy may increase the rate of T2D remission compared with non-surgical standard care in patients with T2D and a BMI <35 kg/m² during 1-3 years follow-up. Low certainty of evidence (GRADE ⊕⊕○○).

Diabetes related complications (neuropathy, nephropathy, retinopathy)

The outcome was not studied.

Cardiovascular complications (i.e. stroke or acute coronary event)

The outcome was not studied.

Health-related quality of life (HRQoL) (Appendix 4:3)

Health-related quality of life was studied in one RCT (n= 51). Physical wellbeing, as measured with SF-36, improved significantly two years after bariatric surgery (laparoscopic adjustable gastric band) compared with medical treatment (p<0.0001). Mental wellbeing (SF-36) did not differ significantly between the study groups.

Conclusion: Bariatric surgery may increase HRQoL regarding physical well-being and may result in little or no difference regarding mental well-being compared with medical treatment in patients with T2D and a BMI <35 kg/m². Low certainty of evidence (GRADE ⊕⊕○○).

Outcomes important for decision making

Glycaemic control (HbA1c) (Appendix 4:4)

Mean changes in HbA1c were evaluated in four RCTs and six cohort studies (two reporting on the same material). Follow-up in the RCTs was 1-3 years (n=231). Bariatric surgical techniques included RYGB, sleeve gastrectomy, gastric banding and duodenal-jejunal bypass surgery with minimal gastric resection, while the control groups were treated with standard, intensive medical or multidisciplinary care. Follow-up in the cohort studies was 1-3 years (n=208). Surgery included sleeve gastrectomy, duodenal-jejunal bypass, RYGP or biliopancreatic diversion, and the control groups were treated with standard medical care. The mean changes in HbA1c in the four RCTs were -0.8 to -4.5 percent units in surgical and 0.1 to -3.42 percent units in the control groups, with significantly different intergroup change in three of the four RCTs (p from <0.05 to 0.0013).

In the cohort studies, the mean changes in HbA1c were -0.9 to -3.6 percent units in surgical and 0.7 to -1.6 percent units in control group patients. The p-values for intergroup difference for of HbA1c at follow-up were reported in two studies and was statistically significant in one of these.

Conclusion: Bariatric surgery compared with non-surgical standard treatment probably reduces HbA1c compared with non-surgical standard care in patients with T2D and a BMI <35 kg/m² during 1-3 years follow-up. Moderate certainty of evidence (GRADE ⊕⊕⊕○).

Outcomes less important for decision making

Other risk factors (dyslipidemia, hypertension, sleep apnoea) (Appendix 4:5)

Other metabolic risk factors included dyslipidaemia, hypertension, sleep apnoea, inflammatory mediators and adiponectin, some or all of which were reported in two RCT and six cohort studies (two reporting on the same material) (n=367). All studies lacked power for this outcome. One RCT had minor while the other RCTs and the cohort studies had major study limitations. Follow-up varied between one and three years. Bariatric surgery compared with medical treatment was reported to have more pronounced effects on blood lipids in two RCTs and five cohort studies although no intergroup comparison was presented. Inflammatory markers, as well as adiponectin, were more favourably regulated by surgery (p-values not stated) compared with usual care + exenatide treatment, and not at all by usual care alone in one RCT (Liang *et al.*, 2013).

Antihypertensive and antihyperlipidemic medications were decreased by surgery (p-values not stated) in three studies whereas they were increased in the medically treated groups.

Conclusion: It is uncertain whether bariatric surgery compared with non-surgical standard treatment improves metabolic risk factors compared with non-surgical standard care in patients with T2D and a BMI <35 kg/m². Very low certainty of evidence (GRADE ⊕○○○).

Body Mass Index (BMI) or body weight (Appendix 4:6)

Effects on BMI were reported in four RCTs and six cohort studies (two reporting on the same material) (n=608). Five different surgical interventions were employed (RYGBP, DJB, SG, AGB, BPD). Follow up varied between one to three years. In four RCT (p<0.001 to < 0.05) and two cohort studies (p<0.0001 to <0.05) significant intergroup differences were seen regarding BMI or weight reduction in favour for surgical treatment compared with no surgery. In four cohort studies p-values for intergroup differences were not stated.

Conclusion: Bariatric surgery compared with non-surgical standard care probably reduces BMI in patients with T2D and a BMI <35 kg/m². Moderate certainty of evidence (GRADE ⊕⊕⊕○).

Fasting plasma glucose (FPG) (Appendix 4:7)

Mean changes in FPG were evaluated in two RCTs and four cohort studies (two reporting on the same material). Follow-up in the two RCTs was 1-2 years (n=74). The surgical treatments were gastric banding or duodenal-jejunal bypass surgery with minimal gastric resection, while the control groups were treated with standard or multidisciplinary care. Follow-up in the cohort studies was 1-3 years (n=174). Surgical techniques included sleeve gastrectomy, duodenal-jejunal bypass, RYGB or biliopancreatic diversion, and the control groups were treated with standard medical care.

In one RCT the mean intergroup difference in treatment effect was 1.9 mmol/l (p=0.0038) favouring gastric banding compared with multidisciplinary care. In the other RCT the FPG difference was -57 mg/dl in the surgery group and -41 mg/dl in the control group (n.s. intergroup difference).

In the four cohort studies the mean changes in FPG within the surgery groups were from -100 to -52 mg/dl, and -1.6 mmol/l in one study, whereas the mean changes within the control groups were from -29 to 15 mg/dl, and -0.6 mmol/l in one study (intergroup p<0.05 in two studies, n.s. in one study, not reported in one study).

Conclusion: Bariatric surgery may reduce fasting plasma glucose compared with non-surgical standard care in patients with T2D and a BMI <35 kg/m² during 1-3 years follow-up.

Low certainty of evidence (GRADE ⊕⊕○○).

Use of glucose lowering medication (Appendix 4:8)

Measures of the use of glucose-lowering treatments were studied in two RCTs and two cohort studies. Follow-up in the two RCTs was 1-3 years (n=72). Surgical techniques included RYGB, sleeve gastrectomy or duodenal-jejunal bypass surgery with minimal gastric resection, while the control groups were treated with standard care or intensive medical treatment. In one RCT there was a non-significant decrease in medication score in both groups (intergroup difference n.s.).

Intergroup difference was not reported in the other RCT.

Follow-up in the two cohort studies was one year (n=102). The surgical treatments were RYGP, or biliopancreatic diversion, and the control groups were treated with standard medical care. In one study 63% of the surgical compared with none of the medically treated patients did not require any glucose-lowering medication (intergroup comparison not reported). In another study, surgically treated patients reduced diabetes medications with 71% compared with 6% in the control group (p <0.001 between groups).

Conclusion: It is uncertain whether glucose-lowering medication is reduced by bariatric surgery compared with non-surgical standard care in patients with T2D and a BMI <35 kg/m².

Very low certainty of evidence (GRADE ⊕○○○).

Complications and risks (Appendix 4:9)

Complications after surgery were reported in four RCTs and five cohort studies (540 patients). The reported frequencies of surgical complications was from four to 17% and ranged from mild, *e.g.* early transient gastroplegia (13.3%) in one study and nausea (16-55.6% in two studies), to more severe such as an anastomotic leak (Petry *et al.*, 2015), internal herniation or unspecified surgical complications (5-11.8%) requiring surgical intervention in individual patients. Intraperitoneal and intestinal bleeding managed conservatively was reported in a few cases (3.3-5%). Stomal/marginal ulcers were reported in 5-11.8% of RYGB patients. One patient underwent cholecystectomy during the follow up period of one year (4%). Hypoglycaemic events before insulin withdrawal were reported in 17% of duodenal-jejunal bypass patients, but were much more common in the control group receiving medical therapy (56%).

In the control groups other reported complications and side effects included *i.e.* vomiting (8-38%), weight gain (>5%) in 16% of patients, requirement of retinal photocoagulation due to diabetes retinopathy (8%) and one case of eosinophilic fasciitis suspected to be caused by Atorvastatin treatment (4%).

10. Ethical issues

Surgically induced weight loss has a well-known positive correlation to improved glycaemic control and a substantial effect on T2D. One critical question is therefore if we are withholding patients with Grade I obesity (BMI 30-34.99 kg/m²) and T2D an effective treatment option? On the other hand, is it acceptable to introduce surgery as a diabetic treatment in individuals with BMI <35kg/m² based on available science? In other words: Is surgery effective? Is it safe?

Although there are data supporting a positive effect of surgery on T2D in the BMI interval 30-34.99 kg/m², no data showing long-term efficacy regarding important outcomes such as end organ disease and mortality rates are available. All types of surgical interventions are associated with a risk of complications and long term adverse effects why a proper risk-benefit analysis is needed.

Furthermore, it is unknown whether the surgical procedure and the linked surveillance procedures are beneficial from a health economical perspective compared with existing standard care for diabetics in this BMI interval.

Offering also patients with BMI 30-34.99 kg/m² bariatric surgery for T2D control will probably demand an expansion of bariatric surgery in Region Västra Götaland. This may cause displacement effects.

11. Organisational aspects

Time frame for the putative introduction of bariatric surgery for diabetes control in adults with BMI<35 kg/m²

The new technology could be introduced rapidly, using available resources and surgical expertise.

Present use of the technology in other hospitals in Region Västra Götaland

Type 2 diabetes with BMI < 35 kg/m² is currently not a criterion for bariatric surgery within public health care in Sweden.

Consequences for personnel of introduction of the new technology

Introduction of this technology would increase the number of patients eligible for bariatric surgery, thus requiring increased resources with respect to all involved health care professions as well as hospital beds.

Consequences for other clinics or supporting functions at the hospital or in Region Västra Götaland

It is difficult to estimate the increase in number of surgical procedures if this technology is introduced. The proportion of T2D patients in this BMI interval that has contraindications to bariatric surgery is not known. The willingness to be subjected to surgery is unknown and new glucose-lowering pharmaceuticals with weight-lowering properties are currently introduced and may in the near future serve as non-surgical alternatives. Currently (2014-2015) the number of patients with T2D (age ≤ 60 years) and BMI 30-34.99 kg/m² is 5,278 (32.3%, proportion previously offered bariatric surgery not known; data from The Swedish National Diabetes Register, NDR).

12. Economic aspects

Present costs of currently used technologies

According to the Swedish National Diabetes Register (Nationella Diabetesregister, NDR) the annual prevalence was approximately 4,300 patients with T2D with a BMI of 30-35 kg/m² in Region Västra Götaland during 2012 to 2015. Although not all patients should be considered for bariatric surgery due to contraindications for the surgery, or that some patients do not want go through with the surgery. The estimation of total annual cost of bariatric surgery is based on that 150 patients undergo the surgery each year.

Keating *et al.*, 2015, followed the health care consumptions during 15 years for patients from the Swedish Obese Subjects (SOS) study. Of the recruited patients, 603 patients had T2D and either had bariatric surgery (n=343) or conventional treatment (n=260). According to the results, patients with T2D and conventional treatment had a mean annual cost per patient of 33,400 SEK. The total annual cost of conventional treatment for 150 patients would be 5.01 million SEK.

Expected costs of bariatric surgery

The cost for bariatric surgery at the Sahlgrenska university hospital is estimated to 75,000 SEK, during the first year. According to the study by Keating *et al.*, 2015, the mean annual cost per patient during year 2-15 was 28,700 SEK. The total annual cost of bariatric surgery for 150 patients would be 15.55 million SEK.

Total change of cost

The total annual change of cost per patient who had bariatric surgery in comparison of conventional treatment is the cost of the bariatric surgery and the cost saving of drug consumption (Table 2). According to Keating *et al.*, 2015, the difference between in cost of inpatient care and outpatient care was not statistical significant between the two groups, when the cost for the surgery were excluded.

The total change of cost for 150 patients would be an additional cost of 11.25 million SEK of the bariatric surgery and a cost saving of 585,000 SEK due to lower cost of drug consumption.

Table 2. Annual cost per patient (SEK) after bariatric surgery and conventional treatment

	Surgery	Conventional	Change in costs
Bariatric surgery	75,000	-	75,000
Inpatient care cost year 2-15	21,500	22,200	n.s.
Year 2-6	25,200	23,800	n.s.
Year 7-15	17,900	20,600	n.s.
Outpatient care cost year 2-15	5,800	5,900	n.s.
Year 2-6	4,000	3,100	n.s.
Year 7-15	6,400	7,600	n.s.
Drug cost year 7-15*	1,400	5,300	-3,900
Total cost	103,700	33,400	71,100

Source: Keating *et al.*, 2015. * Registry data for drug costs for year 2-6 not reported. n.s.: not significant. Rate: 7 SEK = US\$1.

Possibility to adopt and use the new technology within the present budget

The expected costs are not covered in the current budget

Available economic evaluations or cost advantages/disadvantages

No health economic or cost analyses were available.

13. Discussion

Summary of main results

The current systematic review aimed at analysing the certainty of evidence supporting the use of bariatric surgery as treatment of T2D in patients with BMI <35 kg/m². The review shows that bariatric surgery may increase the frequency of T2D remission compared with medical treatment, and probably results in an improved glycaemic control, measured as HbA1c. However, there are no long term (>3 year follow up) studies in this particular group of patients. Effects on the critical outcomes mortality and cardiovascular morbidity are poorly studied. There are no studies on diabetic complications. The effects on other metabolic risk factors are uncertain.

Overall completeness and applicability of evidence

The scientific basis for using bariatric surgery in patients with T2D and BMI <35 kg/m² is still very limited with respect to the number of patients and the duration of follow-up. The patients in the currently included studies, however, generally seemed to be representative of this group of patients in Swedish clinical practice. The present analysis showed beneficial effects mainly on weight and glycaemic control (HbA1c) by bariatric surgery compared with medical treatment. The effects on other outcomes are uncertain. Furthermore, it should be noted that the bariatric procedures mainly performed in Sweden today (Roux-en-Y gastric bypass and vertical sleeve gastrectomy) were investigated in only half of the current studies.

Agreements and disagreements with other studies and reviews

Various HTA reports and systematic reviews have examined the effect of bariatric surgical procedures on T2D (e.g. Giske *et al.*, 2014; NICE, 2014). The present HTA report adds a systematic review and quality assessment of all available controlled studies in patients in the lower BMI interval (Grade I obesity). The results are generally in good agreement with those in the recently published joint statement (Rubino *et al.*, 2016).

Knowledge gaps

Data on long term efficacy and safety are lacking. Furthermore, there are no results indicating reduced risk of cardiovascular disease, cancer or death.

14. Future perspective

Scientific knowledge gaps

There is a need for large controlled studies with long-term follow up, powered to address effects on cardiovascular disease and death. Such studies should preferably include comparison with pharmacological risk factor treatment e.g. the recently launched SGLT-2 inhibitors and GLP-1 receptor agonists, which have been shown to reduce cardiovascular risk and mortality in patients with T2D at high cardiovascular risk. In addition, it is important to evaluate predictors of positive results of bariatric surgery in order to improve patient selection.

Ongoing research

A search in Clinicaltrials.gov 2016-05-09 using the search string ((Bariatric surger* OR Bariatric operation* OR Bariatric surgical procedure* OR Bariatric procedure* OR Biliopancreatic diversion OR Bilio-pancreatic diversion OR Biliopancreatic bypass OR Duodenojejunal bypass OR Duodenal jejunal bypass OR Duodenal switch OR Gastric bypass OR Gastroplast* OR Gastric band* OR Gastric sleeve* OR Gastric surgery OR Gastroenterostom* OR Gastrojejunostom* OR Ileal interposition OR Jejunoleal bypass OR Lap-band* OR Metabolic surger* OR Obesity surgery OR Roux-en-Y gastric bypass OR Roux-en Y OR Sleeve gastrectomy) AND (Diabet* OR T2DM OR Diabetes Mellitus, Type 2) AND (Body mass index OR BMI)) identified 76 trials. Ten of them were relevant to the here addressed question, focusing on the effect of bariatric surgery on T2D control in patients with Grade I obesity (Table 3). One of the trials is a continuation of a report already discussed in this report (STAMPEDE, NCT00432809, see Schauer *et al.*, 2014). The five year follow up results of this study is to be published within the next couple of months.

Table 3. Registered trials in Clinicaltrials.gov on bariatric surgery for T2D control

Clinical trials no	Title	Status
NCT01046994	Prospective Controlled Trial on Surgical Treatment of Type 2 Diabetes Patients With BMI 25-30 by Means of Biliopancreatic Diversion	Recruiting
NCT00432809	Advanced Medical Therapy Versus Advanced Medical Therapy Plus Bariatric Surgery for the Resolution of Type 2 Diabetes	Active, not recruiting
NCT02041234	Roux-en-Y Gastric Bypass for BMI 27-32 Type 2 Diabetes Versus Best Medical Treatment	Recruiting
NCT01041768	Multicentric Prospective Randomized Trial on Surgery Versus Standard Medical Care in Type 2 Diabetic Patients BMI 30-35	Recruiting
NCT01197963	A Surgical Approach to the Management of Type II Diabetes Mellitus in Patients With a BMI Between 25-35 kg/m ²	Terminated
NCT02036138	The Efficacy of Bariatric Surgery Compared to Medical Therapy in Controlling Type2 Diabetes Mellitus in Patients With Non Morbid Obesity.	Recruiting
NCT02610530	Surgical Intervention for the Treatment of Diabetes in Overweight Non-responders-1	Enrolling by invitation
NCT00965302	Sleeve Gastrectomy Versus Medical Management for Remission of Diabetes in Mild to Moderately Obese Patients	Completed
NCT01821508	Clinical Study on Metabolic Surgery Compared to the Best Clinical Treatment in Patients With Type 2 Diabetes Mellitus	Recruiting
NCT01231308	Roux-en-Y-Gastric Bypass vs. Lifestyle Modification and Medical Therapy in the Treatment of Type 2 Diabetes	Recruiting

15. Participants in the project

The question was nominated by

Hans Lönroth, Area Director, Sahlgrenska University Hospital, Gothenburg, Sweden

Participating health care professionals

Lars Fändriks, MD, Professor, Department of Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden, and Department of Gastrosurgical Research and Education, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Björn Eliasson, MD, Professor, Department of Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden

Madeléne Sandqvist, MD, PhD, Department of Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden

Ville Wallenius, MD, Assoc. Professor, Department of Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden

Participants from the HTA-centrum

Petteri Sjögren, DDS, PhD, HTA-centrum, Region Västra Götaland, Sahlgrenska University Hospital, Gothenburg, Sweden

Lennart Jivegård, MD, PhD, Associate Professor, Senior University Lecturer, HTA-centrum, Region Västra Götaland, Sahlgrenska University Hospital, Gothenburg, Sweden

Eva-Lotte Daxberg, Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden

Maud Eriksson, Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden

Josefine Persson, Health economist, MSc, HTA-centrum, Region Västra Götaland, Sahlgrenska University Hospital, Gothenburg, Sweden

External reviewers

Christian Rylander, MD, PhD, Department of Anesthesia / Surgery / Intensive Care Sahlgrenska University Hospital, Gothenburg, Sweden

Carl-Johan Behre, MD, Associate professor, Department of Cardiology, Sahlgrenska University Hospital, Gothenburg, Sweden

Declaration of interest

None

Project time

HTA was accomplished during the period of 2016-01-13– 2016-10-26.

Literature searches were made in January 2016

Appendix 1: Search strategy, study selection and references

The focused question

Is bariatric surgery in patients with type 2 diabetes mellitus and a BMI <35 kg/m² superior to standard treatment with regard to diabetes control?

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

P: Adult patients with type 2 diabetes mellitus (T2D) and BMI <35 kg/m²

I: Bariatric surgery (e.g. Roux-en-Y Gastric Bypass, Vertical Sleeve Gastrectomy) + Non-surgical standard care (e.g. life style changes and pharmaceuticals)

C: Non-surgical standard care (e.g. life style changes and pharmaceuticals)

O: Critical for decision-making

Mortality

Remission from T2D

Diabetes related complications

Cardiovascular complications

Health related quality of life

Important for decision-making

Glycaemic control (HbA1c)

Less important for decision making

Other risk factors (dyslipidaemia, hypertension, sleep apnoea)

BMI, body weight, waist circumference

Fasting plasma glucose

Use of blood glucose lowering medication

Complications and risks

Eligibility criteria

Study design: RCT, non-randomised controlled studies, case-series (n >500), for complications and risks.

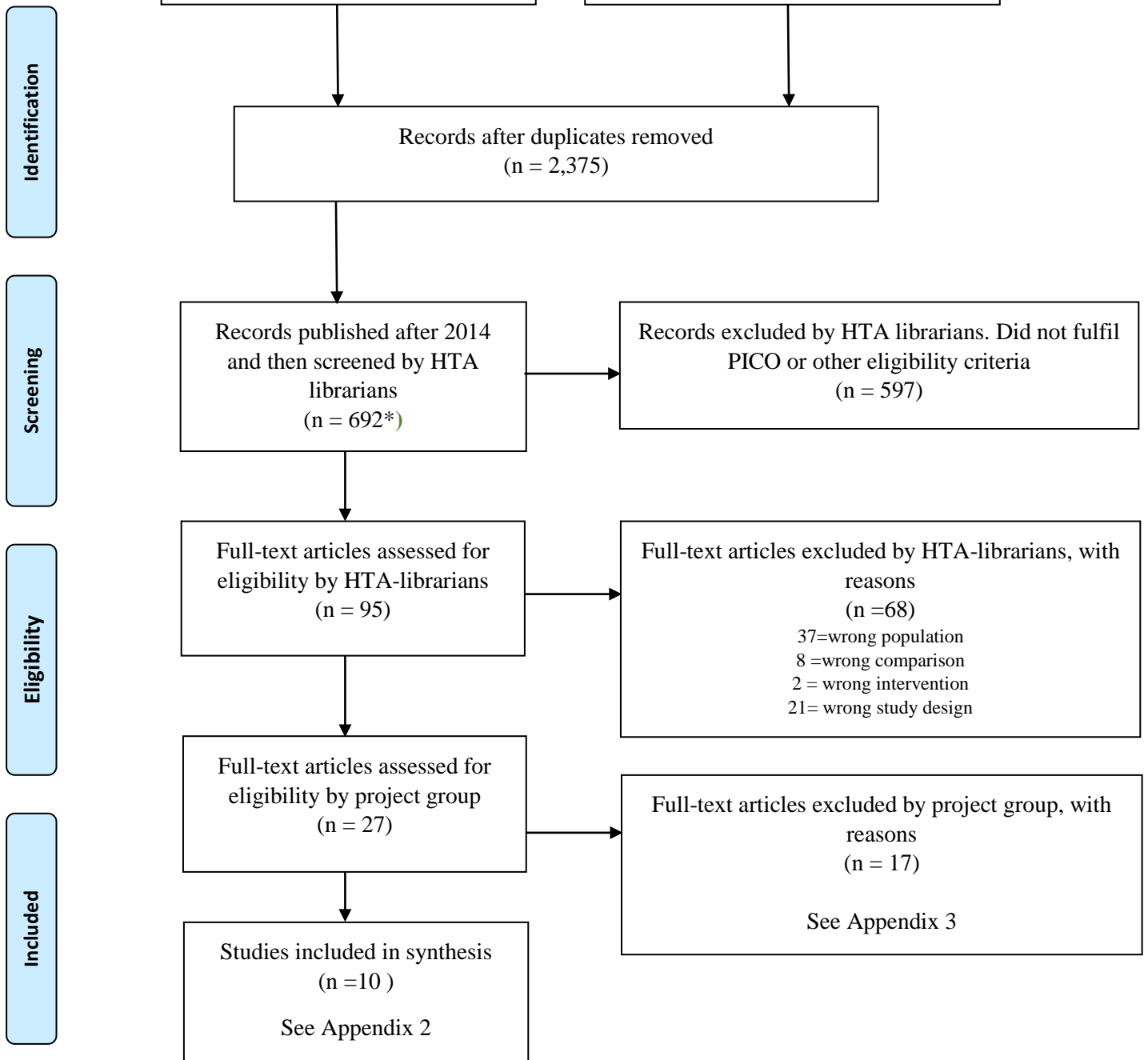
Publication year:

2000- and SR from 2014 and onwards for complete control of the literature search and use in discussion.

Language: English, Scandinavian languages

Follow-up: at least 1 year

Selection process – flow diagram



* It was decided to only screen studies published after systematic reviews with last date of searches in 2014. In addition, primary publications included in those systematic reviews were also screened for inclusion, resulting in a total of 692 records screened.

Search strategies

Database: PubMed

Date: 2016-01-18

No of results: 1547

Search	Query	Items found
#25	Search #15 NOT #18 Filters: Publication date from 2000/01/01; Danish; English; Norwegian; Swedish	1547
#24	Search #15 NOT #18 Filters: Danish; English; Norwegian; Swedish	1587
#19	Search #15 NOT #18	1704
#18	Search #16 OR #17	1338836
#17	Search Child[ti] OR children[ti] OR pediatric*[ti] OR paediatric*[ti] OR infant*[ti]	767685
#16	Search ((child[mh]) NOT (child[mh] AND adult[mh]))	1031614
#15	Search #11 NOT #14	1724
#14	Search #12 OR #13	4373146
#13	Search animals[ti] OR animal[ti] OR rats[ti] OR rat[ti] OR mouse[ti] OR mice[ti]	1274458
#12	Search ((animals[mh]) NOT (animals[mh] AND humans[mh]))	4168239
#11	Search #9 NOT #10	1726
#10	Search (Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp])	1450774
#9	Search #6 AND #7 AND #8	1753
#8	Search Body mass index[Mh] OR Body mass index[tiab] OR BMI[tiab]	189046
#7	Search Diabet*[tiab] OR T2DM[tiab] OR Diabetes Mellitus, Type 2[Mh]	479626
#6	Search #1 OR #2 OR #3 OR #4 OR #5	33973
#5	Search Metabolic surger*[tiab] OR Obesity/surgery[mh] OR Obesity surgery[tiab] OR Roux-en-Y gastric bypass[tiab] OR Roux-en Y[tiab] OR Sleeve gastrectomy[tiab]	17930
#4	Search Ileal interposition[tiab] OR Jejunioleal bypass[tiab] OR Lap-band*[tiab]	1145
#3	Search Gastric bypass[mh] OR Gastric bypass[tiab] OR Gastroplasty[mh] OR Gastroplast*[tiab] OR Gastric band*[tiab] OR Gastric sleeve*[tiab] OR Gastric surgery[tiab] OR Gastroenterostomy[mh] OR Gastroenterostom*[tiab] OR Gastrojejunostom*[tiab]	18773
#2	Search Biliopancreatic diversion[tiab] OR Bilio-pancreatic diversion[tiab] OR Biliopancreatic bypass[tiab] OR Duodenojejunal bypass[tiab] OR Duodenal jejunal bypass[tiab] OR Duodenal switch[tiab]	1286
#1	Search Bariatric surgery[mh] OR Bariatric surger*[tiab] OR Bariatric operation*[tiab] OR Bariatric surgical procedure*[tiab] OR Bariatric procedure*[tiab]	20282

Database: Cochrane

Date: 2016-01-18

No of results: 298

Cochrane Reviews (89)

Other Reviews (20)

Trials (167)

Method Studier (0)

Technology Assessment (8)

Economic Evaluations (12)

Cochrane Groups (2)

ID	Search	Hits
#1	Bariatric surger* or Bariatric operation* or Bariatric surgical procedure* or Bariatric procedure* (Word variations have been searched)	904
#2	Biliopancreatic diversion or Bilio-pancreatic diversion or Biliopancreatic bypass or Duodenojejunal bypass or Duodenal jejunal bypass or Duodenal switch (Word variations have been searched)	154
#3	"Gastric bypass" or Gastroplast* or Gastric band* or Gastric sleeve* or "Gastric surgery" or Gastroenterostom* or Gastrojejunostom* (Word variations have been searched)	1710
#4	"Ileal interposition" or "Jejunoileal bypass" or Lap-band* (Word variations have been searched)	104
#5	"Metabolic surgery" or "Obesity surgery" or "Roux-en-Y gastric bypass" or "Roux-en Y" or "Sleeve gastrectomy" (Word variations have been searched)	1072
#6	#1 or #2 or #3 or #4 or #5	2513
#7	Diabet* or T2DM (Word variations have been searched)	45812
#8	"Body mass index" or BMI (Word variations have been searched)	23428
#9	#6 and #7 and #8 Publication Year from 2000 to 2016	298

Database: Embase 1974 to 2016 (via OVID)

Date: 2016-01-18

No of results: 1709

#	Searches	Results
1	exp bariatric surgery/	24029
2	exp gastric sleeve/	289
3	exp jejunoileostomy/	758
4	jejunoileal bypass/	652
5	jejunostomy/	4029
6	exp stomach surgery/	86183
	(Bariatric surger* or Bariatric operation* or Bariatric surgical procedure* or Bariatric procedure* or Biliopancreatic diversion or Bilio-pancreatic diversion or Biliopancreatic bypass or Duodenojejunal bypass or Duodenal jejunal bypass or Duodenal switch or Gastric bypass or Gastroplast* or Gastric band* or Gastric sleeve* or Gastric surgery or Gastroenterostom* or Gastrojejunostom* or Ileal interposition or Jejunoileal bypass or Lap-band* or Metabolic surger* or Obesity surgery or Roux-en-Y gastric bypass or Roux-en Y or Sleeve gastrectomy).ti,ab.	39000
8	1 or 2 or 3 or 4 or 5 or 6 or 7	108278
9	exp non insulin dependent diabetes mellitus/	168452
10	(Diabet* or T2DM).ti,ab.	665251
11	9 or 10	691686
12	exp body mass/	235363
13	("body mass index" or BMI).ti,ab.	266526
14	12 or 13	338104
15	8 and 11 and 14	4511
16	limit 15 to (article or conference paper or note or "review")	2274
17	(animals or animal or rats or rat or mouse or mice or rodent*).ti,ab.	3164001

18	(16 not (animals or animal or rats or rat or mouse or mice or rodent*)).ti,ab.	2231
19	(child not (child and adult)).sh.	975122
20	18 and 19	19
21	18 not 20	2212
22	limit 21 to (danish or english or norwegian or swedish)	2069
23	limit 22 to yr="2000 -Current"	2035
24	limit 23 to (embase and yr="2000 -Current")	1781
25	(Child or children or pediatric* or paediatric* or infant*).ti,ab.	1636710
26	24 not 25	1709

Database: CRD

Date: 2016-01-20

No of results: 46

Line	Search	Hits
1	(Bariatric surger* OR Bariatric operation* OR Bariatric surgical procedure* OR Bariatric procedure* OR Biliopancreatic diversion OR Bilio-pancreatic diversion OR Biliopancreatic bypass OR Duodenojejunal bypass OR Duodenal jejunal bypass OR Duodenal switch OR Gastric bypass OR Gastroplast* OR Gastric band* OR Gastric sleeve* OR Gastric surgery OR Gastroenterostom* OR Gastrojejunostom* OR Ileal interposition OR Jejunoileal bypass OR Lap-band* OR Metabolic surger* OR Obesity surgery OR Roux-en-Y gastric bypass OR Roux-en Y OR Sleeve gastrectomy) FROM 2000 TO 2016	401
2	(diabet*) OR (T2DM) FROM 2000 TO 2016	4062
3	(body mass index) OR (BMI) FROM 2000 TO 2016	1090
4	#1 AND #2 AND #3	46

Reference lists

A comprehensive review of reference lists brought 47 new records.

The web-sites of **SBU**, **Kunnskapssenteret** and **Sundhedsstyrelsen** were visited

2016-01-20, one study, relevant to the question at issue, was found.

Reference lists

Included studies:

Abbatini F, Capoccia D, Casella G, Coccia F, Leonetti F, Basso N. Type 2 diabetes in obese patients with body mass index of 30-35 kg/m²: sleeve gastrectomy versus medical treatment. *Surg Obes Relat Dis.* 2012; 8(1):20-4.

Geloneze B, Geloneze SR, Chaim E, Hirsch FF, Felici AC, Lambert G, et al. Metabolic surgery for non-obese type 2 diabetes: Incretins, adipocytokines, and insulin secretion/resistance changes in a 1-year interventional clinical controlled study. *Ann Surg.* 2012; 256(1):72-8.

Liang Z, Wu Q, Chen B, Yu P, Zhao H, Ouyang X. Effect of laparoscopic Roux-en-Y gastric bypass surgery on type 2 diabetes mellitus with hypertension: A randomized controlled trial. *Diabetes Res Clin Pract.* 2013; 101(1):50-6.

Petry TZ, Fabbrini E, Otoch JP, Carmona MA, Caravatto PP, Salles JE, et al. Effect of duodenal-jejunal bypass surgery on glycemic control in type 2 diabetes: A randomized controlled trial. *Obesity.* 2015; 23(10):1973-9.

Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Brethauer SA, Navaneethan SD, et al. Bariatric surgery versus intensive medical therapy for diabetes--3-year outcomes. *N Engl J Med.* 2014; 370(21):2002-13.

Scopinaro N, Adami GF, Papadia FS, Camerini G, Carlini F, Briatore L, et al. Effects of gastric bypass on type 2 diabetes in patients with BMI 30 to 35. *Obes Surg.* 2014; 24(7):1036-43.

Scopinaro N, Adami GF, Papadia FS, Camerini G, Carlini F, Briatore L, et al. The effects of biliopancreatic diversion on type 2 diabetes mellitus in patients with mild obesity (BMI 30-35 kg/m²) and simple overweight (BMI 25-30 kg/m²): a prospective controlled study. *Obes Surg.* 2011a; 21(7):880-8.

Scopinaro N, Adami GF, Papadia FS, Camerini G, Carlini F, Fried M, et al. Effects of biliopancreatic diversion on type 2 diabetes in patients with BMI 25 to 35. *Ann Surg.* 2011b; 253(4):699-703.

Serrot FJ, Dorman RB, Miller CJ, Slusarek B, Sampson B, Sick BT, et al. Comparative effectiveness of bariatric surgery and nonsurgical therapy in adults with type 2 diabetes mellitus and body mass index <35 kg/m². *Surgery.* 2011; 150(4):684-91.

Wentworth JM, Playfair J, Laurie C, Ritchie ME, Brown WA, Burton P, et al. Multidisciplinary diabetes care with and without bariatric surgery in overweight people: A randomised controlled trial. *The Lancet Diabetes and Endocrinology.* 2014; 2(7):545-52.

Excluded studies:

Borisenko O, Adam D, Funch-Jensen P, Ahmed AR, Zhang R, Colpan Z, et al. Bariatric Surgery can Lead to Net Cost Savings to Health Care Systems: Results from a Comprehensive European Decision Analytic Model. *Obes Surg.* 2015; 25(9):1559-68.

Celik A, Asci M, Celik BO, Ugale S. The impact of laparoscopic diverted sleeve gastrectomy with ileal transposition (DSIT) on short term diabetic medication costs. *Springerplus.* 2015 Aug 14;4:417. doi: 10.1186/s40064-015-1216-z. eCollection 2015

Chiellini C, Rubino F, Castagneto M, Nanni G, Mingrone G. The effect of bilio-pancreatic diversion on type 2 diabetes in patients with BMI <35 kg/m². *Diabetologia.* 2009; 52(6):1027-30.

Courcoulas AP, Belle SH, Neiberg RH, Pierson SK, Eagleton JK, Kalarchian MA, et al. Three-Year Outcomes of Bariatric Surgery vs Lifestyle Intervention for Type 2 Diabetes Mellitus Treatment: A Randomized Clinical Trial. *JAMA Surg.* 2015; 150(10):931-40.

Courcoulas AP, Goodpaster BH, Eagleton JK, Belle SH, Kalarchian MA, Lang W, et al. Surgical vs medical treatments for type 2 diabetes mellitus: a randomized clinical trial. *JAMA Surg.* 2014; 149(7):707-15.

DePaula AL, Stival AR, DePaula CC, Halpern A, Vencio S. Surgical treatment of type 2 diabetes in patients with BMI below 35: mid-term outcomes of the laparoscopic ileal interposition associated with a sleeve gastrectomy in 202 consecutive cases. *J Gastrointest Surg.* 2012;16(5):967-76.

Ding SA, Simonson DC, Wewalka M, Halperin F, Foster K, Goebel-Fabbri A, et al. Adjustable Gastric Band Surgery or Medical Management in Patients With Type 2 Diabetes: A Randomized Clinical Trial. *J Clin Endocrinol Metab.* 2015; 100(7):2546-56.

Dixon JB, O'Brien PE, Playfair J, Chapman L, Schachter LM, Skinner S, et al. Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. *JAMA.* 2008; 299(3):316-23.

Halperin F, Ding SA, Simonson DC, Panosian J, Goebel-Fabbri A, Wewalka M, et al. Roux-en-Y gastric bypass surgery or lifestyle with intensive medical management in patients with type 2 diabetes: Feasibility and 1-year results of a randomized clinical trial. *JAMA Surgery.* 2014; 149(7):716-26.

Ikramuddin S, Billington CJ, Lee WJ, Bantle JP, Thomas AJ, Connett JE, et al. Roux-en-Y gastric bypass for diabetes (the Diabetes Surgery Study): 2-year outcomes of a 5-year, randomised, controlled trial. *The Lancet Diabetes and Endocrinology.* 2015; 3(6):413-22.

Ikramuddin S, Korner J, Lee WJ, Connett JE, Inabnet WB, Billington CJ, et al. Roux-en-Y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: the Diabetes Surgery Study randomized clinical trial. *JAMA.* 2013; 309(21):2240-9.

Kashyap SR, Bhatt DL, Wolski K, Watanabe RM, Abdul-Ghani M, Abood B, et al. Metabolic effects of bariatric surgery in patients with moderate obesity and type 2 diabetes: Analysis of a randomized control trial comparing surgery with intensive medical treatment. *Diabetes Care.* 2013;36(8):2175-82.

Keating C, Neovius M, Sjöholm K, Peltonen M, Narbro K, Eriksson JK, et al. Health-care costs over 15 years after bariatric surgery for patients with different baseline glucose status: results from the Swedish Obese Subjects study. *Lancet Diabetes Endocrinol.* 2015; 3(11):855-65.

Malin SK, Samat A, Wolski K, Abood B, Pothier CE, Bhatt DL, et al. Improved acylated ghrelin suppression at 2 years in obese patients with type 2 diabetes: Effects of bariatric surgery vs standard medical therapy. *Int J Obes.* 2014; 38(3):364-70.

Schauer PR, Kashyap SR, Wolski K, Brethauer SA, Kirwan JP, Pothier CE, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. *N Engl J Med.* 2012;366(17):1567-76.

Sjöholm K, Anveden A, Peltonen M, Jacobson P, Romeo S, Svensson PA, et al. Evaluation of current eligibility criteria for bariatric surgery: diabetes prevention and risk factor changes in the Swedish obese subjects (SOS) study. *Diabetes Care.* 2013; 36(5):1335-40.

Sjöholm K, Pajunen P, Jacobson P, Karason K, Sjöstrom CD, Torgerson J, et al. Incidence and remission of type 2 diabetes in relation to degree of obesity at baseline and 2 year weight change: the Swedish Obese Subjects (SOS) study. *Diabetologia.* 2015; 58(7):1448-53.

Other references

Aminian A, Brethauer SA, Andalib A, Puchai S, Mackey J, Rodriguez J et al. Can Sleeve Gastrectomy "Cure" Diabetes? Long-term Metabolic Effects of Sleeve Gastrectomy in Patients with Type 2 Diabetes. *Ann Surg.* 2016 Oct; 264(4):674-81.

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ*. 2004 Jun 19; 328(7454):1490-4.

Carlsson LM, Peltonen M, Ahlin S, Anveden Å, Bouchard C, Carlsson B et al. Bariatric surgery and prevention of type 2 diabetes in Swedish obese subjects. *N Engl J Med*. 2012 Aug 23; 367(8):695-704.

[Checklists from SBU regarding randomized controlled trials. [Internet]. [cited 2016 Sept 30] Available from: https://www2.sahlgrenska.se/upload/SU/HTA-centrum/Hj%c3%a4lpmedel%20under%20projektet/B02_Granskningsmall%20f%c3%b6r%20%20randomiserad%20kontrollerad%20pr%c3%b6vning%20RCT%202014-10-29.doc

[Checklist from SBU regarding cohort studies]. [Internet]. [cited 2016 Sept 30] Available from: https://www2.sahlgrenska.se/upload/SU/HTA-centrum/Hj%c3%a4lpmedel%20under%20projektet/B03_Granskningsmall%20f%c3%b6r%20kohortstudier%20med%20kontrollgrupp%202014-10-29.doc

Eliasson B, Larsson I, Liljegren A, Samuelsson O, Sandqvist M, Svanberg T, Werling M, Wiklund M, Bergh C. Non-surgical treatment of obesity and overweight. [Internet]. Gothenburg: The Regional Health Technology Assessment Centre (HTA-centrum), Region Vastra Gotaland, 2015. [cited 2016 Sept 30] Available from: <https://www2.sahlgrenska.se/upload/SU/HTA-centrum/HTA-rapporter/HTA-rapport%20Icke-kirurgisk%20behandling%20av%20fetma%20och%20o%CC%88vervikt%202016-01-28%20till%20publicering%20.pdf>

NIH. Gastrointestinal Surgery for Severe Obesity. [Internet]. NIH Consensus Statement Online 1991 Mar 25-27(1):1-20. [cited 2016 Sept 29]. Available from: <https://consensus.nih.gov/1991/1991GISurgeryObesity084html.htm>

Ganz ML, Wintfeld N, Li Q, Alas V, Langer J, Hammer M. The association of body mass index with the risk of type 2 diabetes: a case-control study nested in an electronic health records system in the United States. *Diabetol Metab Syndr*. 2014 Apr 3;6(1):50. doi: 10.1186/1758-5996-6-50

Giske L, Lauvrak V, Elvsaa I, Hofmann B, Håvelsrud K, Vang V. et al. Langtidseffekter etter fedmekirurgi. Rapport fra Kunnskapssenteret nr. 1-2014. Oslo: Nasjonalt kunnskapssenter for helsetjenesten, 2014.

GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ*. 2004 Jun 19; 328(7454):1490-4.

GRADE Working Group. List of GRADE working group publications and grants [Internet]. [Place unknown]: GRADE Working Group, c2005-2009. [Internet]. [cited 2016 Sept 30]. Available from: <http://www.gradeworkinggroup.org/>

Himpens J, Dobbeleir J, Peeters G. Long-term results of laparoscopic sleeve gastrectomy for obesity. *Ann Surg*. 2010 Aug; 252(2):319-24.

IDF Diabetes Atlas [Internet]. Bryssel: International Diabetes Federation, 2015. [cited 2016 Sept 30] Available from: <http://www.diabetesatlas.org/>

Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2015 Jan;38(1):140-9.

Jansson SP, Andersson DK, Svärdsudd K. Prevalence and incidence rate of diabetes mellitus in a Swedish community during 30 years of follow-up. *Diabetologia*. 2007 Apr; 50(4):703-10.

Keating C, Neovius M, Sjöholm K, Peltonen M, Narbro K, Eriksson JK, et al. Health-care costs over 15 years after bariatric surgery for patients with different baseline glucose status: results from the Swedish Obese Subjects study. *Lancet Diabetes Endocrinol*. 2015; 3(11):855-65.

Lönroth H, Stenlöf K, Fändriks L, Olbers T. Obesitaskirurgi: mini-HTA [Internet]. Göteborg: Västra Götalandsregionen, Sahlgrenska Universitetssjukhuset, HTA-centrum; 2008. HTA-rapport 2008:09. [cited 2016 Sept 30]. Available from: <https://www2.sahlgrenska.se/upload/SU/HTA-centrum/HTA%20Obesitaskirurgi%202008-05-27.pdf>

National Institute for Health and Clinical Excellence (2014) Obesity: identification, assessment and management of overweight and obesity in children, young people and adults: Partial update of CG43: Methods, evidence and recommendations, November 2014.

National Board of Health and Welfare. Nationella riktlinjer för diabetesvård – stöd för styrning och ledning [Internet]. Stockholm: Socialstyrelsen; 2015. [cited 2016 Oct 05]. Available from: <http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/19689/2015-2-3.pdf>

Pories WJ, Swanson MS, MacDonald KG, Long SB, Morris PG, Brown BM et al. Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. *Ann Surg*. 1995 Sep; 222(3):339-50; discussion 350-2.

Rubino F, Nathan DM, Eckel RH, Schauer PR, Alberti KG, Zimmet PZ et al. Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations. *Diabetes Care*. 2016 Jun; 39(6):861-77.

Sjöström L. Review of the key results from the Swedish Obese Subjects (SOS) trial - a prospective controlled intervention study of bariatric surgery. *J Intern Med*. 2013 Mar; 273(3):219-34.

WHO. Obesity and overweight: Fact sheet. [Internet]. Updated June 2016. Geneva: World Health Organization, 2016. [cited 2016 Sept 29] Available from: <http://www.who.int/mediacentre/factsheets/fs311/en/>

The Swedish National Diabetes Register. Nationella Diabetesregistret. NDR. [Internet]. Göteborg (Sweden): Registercentrum Västra Götaland, c1996 [cited 2016 Oct 18]. Available from: <https://www.ndr.nu/#/>

Bariatric surgery for diabetes control in adults with BMI < 35 kg/m²

Appendix 2 – Characteristics of included studies

Author, Year, country	Study Design	Study Duration (years)	Study Groups; Intervention vs control	Patients (n) BMI criteria (kg/m ²)	Mean Age (SD), years [BMI (SD)]	Men (%)	Outcome variables
Liang, 2013, China	RCT	1 year	RYGB vs Usual care vs Exenatide + Usual care	n=108 BMI >28	50.8 (5.4) [30.48 (0.94)] vs 51.8 (6.7) [30.34 (1.96)] vs 50.9 (5.9) [30.28 (1.44)]	69%	Mortality Diabetes remission Glycemic control (HbA1c) Dyslipidemia BMI Treatment complications
Petry, 2015, Brazil (data analysed in USA)	RCT	1 year	DJBM vs Standard care	n=23 BMI 25-29.9 or BMI 30-39.9	47 (8) [29.7 (1.9)] vs 44 (5) [31.7 (3.5)]	Not stated	Diabetes remission Glycemic control (HbA1c) Dyslipidemia Body weight fP-Glucose Diabetes medication needs Treatment complications
Schauer, 2014, USA	RCT	3 years	RYGB + intensive medical treatment vs Sleeve gastrectomy + intensive medical treatment vs Intensive medical treatment	n=150 BMI 27-43	48 (8.45) [37.1 (3.39)] BMI<35: 27% vs 47.8 (8.08) [36.1 (3.91)] BMI<35: 37% vs 50.3 (7.51) [36.4 (2.99)] BMI<35: 45%	68%	Glycemic control (HbA1c) Dyslipidemia BMI Diabetes medication needs Treatment complications

Bariatric surgery for diabetes control in adults with BMI < 35 kg/m²

Appendix 2 – Characteristics of included studies

Author, Year, country	Study Design	Study Duration (years)	Study Groups; Intervention vs control	Patients (n) BMI criteria (kg/m ²)	Mean Age (SD), years [BMI (SD)]	Men (%)	Outcome variables
Wentworth, 2014, Australia	RCT	2 years	Gastric banding + multidisciplinary care vs Multidisciplinary care	n=51 BMI 25-30	53 (6) [29 (1)] vs 53 (7) [29 (1)]	29%	Diabetes remission Health related quality of life Glycemic control (HbA1c) Dyslipidemia BMI fP-Glucose Treatment complications
Abbatini, 2012, Italy	Cohort	1 year	Laparoscopic sleeve gastrectomy vs Conventional medical therapy	n=18 BMI<35	45.5 (12) [32.7 (3.2)] vs 55.8 (6.4) [32.9 (2.0)] p=0.003 (age between groups)	33%	Diabetes remission Glycemic control (HbA1c) Dyslipidemia Hypertension Sleep apnea BMI fP-Glucose Treatment complications
Geloneze, 2012, Brazil	Cohort	1 year	Duodenal-jejunal bypass vs Standard medical care	n=41 BMI 25-29.9	50.0 [26.1 (1.7)] vs 49.8 [26.3 (1.2)]	44%	Glycemic control (HbA1c) Dyslipidemia Hypertension BMI fP-Glucose Treatment complications
Scopinaro, 2014, Italy	Cohort	3 years	RYGB vs Standard medical care	n=47 BMI 30-34.9	57 (?) [32.9 (1.5)] vs 57 (7) [33.0 (1.6)]	74%	Diabetes remission Glycemic control (HbA1c) Dyslipidemia Hypertension BMI fP-Glucose Treatment complications

Author, Year, country	Study Design	Study Duration (years)	Study Groups; Intervention vs control	Patients (n) BMI criteria (kg/m ²)	Mean Age (SD), years [BMI (SD)]	Men (%)	Outcome variables
Scopinaro, 2011a, Italy	Cohort	2 years	Biliopancreatic diversion vs Standard care (results from patients in a database)	n=68 BMI 25-30 or BMI 30-35	<u>Surgical groups:</u> Overweight patients: 57.8 (?) [28.1 (1.4)] Obese patients: 55.0 (?) [33.1 (1.5)] <u>Control groups</u> Overweight patients: 58.8 (7.8) [27.1 (2.1)] Obese patients: 59.5 (8.2) [32.9 (1.8)]	66%	Mortality Glycemic control (HbA1c) Dyslipidemia Hypertension BMI fP-Glucose Treatment complications
Scopinaro, 2011b, Italy	Cohort	1 year	Biliopancreatic diversion vs Standard care (results from patients in a database)	n=68 BMI 25-34.9	56.4 (7.4) [30.6 (2.9)] vs 59 (8) [30.2 (3.5)]	66%	Diabetes remission Glycemic control (HbA1c) Dyslipidemia Hypertension BMI fP-Glucose Diabetes medication needs Treatment complications
Serrot, 2011, USA	Cohort	1 year	RYGB vs Medical management	n=34 BMI<35	Age, median (IQR): 56.0 (7.0) BMI, mean (SD): 34.6 (0.8) vs Age, median (IQR): 62.0 (12.0) BMI, mean (SD): 34.0 (1.0) p=0.05 (age between groups)	44% I: 23.5% C: 64.5% p=0.04 between groups	Diabetes remission Glycemic control (HbA1c) Dyslipidemia Hypertension BMI Diabetes medication needs Treatment complications

I = Intervention. C = Control. RYGB = Laparoscopic Roux-en-Y-gastric bypass. DJBm=Duodenal-jejunal Bypass surgery with minimal gastric resection. BMI=Body Mass Index. fP-Glucose=fasting Plasma Glucose concentration

Appendix 3. Excluded articles – Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Author, publication year	Reason for exclusion
Borisenko, 2015	Wrong P too high BMI
Celik, 2015	Too small case series
Chiellini, 2009	No control group
Courcoulas, 2015	Wrong P too high BMI
Courcoulas, 2014	Wrong P too high BMI
DePaula, 2012	Too small case series
Ding, 2015	Wrong P too high BMI
Dixon, 2008	Wrong P too high BMI
Halperin, 2014	Wrong P too high BMI
Ikramuddin, 2013	Wrong P too high BMI
Ikramuddin, 2015	Wrong P too high BMI
Kashyap, 2013	Wrong P too high BMI
Keating, 2015	Wrong P too high BMI
Malin, 2014	Wrong P too high BMI
Schauer, 2012	No data separated for BMI<35 kg/m ²
Sjöholm, 2013	Wrong P, no diabetes type-2
Sjöholm, 2015	Wrong intervention

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:1

Outcome variable: Mortality

* + No or minor problems ? Some problems - Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Liang, 2013, China	RCT	N=108 I1=34 I2=31 C=36	7	0 (1y)	0 (1y)	I1. Usual + GLP1 (Exenatide) I2. LapRYGB C. Usual care	?	?	-
Scopinaro, 2011a, Italy	Cohort	N=68 I1=15 I2=15 C1=20 C2=18	-	0 (2y)	One fatal heart event in C1 during year 2.	I1. BPD (BMI 30-35) I2. BPD (BMI 25-30) C1. Medicine (BMI 30-35) C2. Medicine (BMI 25-30)	?	?/-	-

LapRYGB, laparoscopic Roux-en-Y gastric bypass; BPD, biliarypancreatic diversion; BMI, body mass index

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:2

Outcome variable: Remission of type-2 diabetes

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Liang, 2013, China	RCT	n=108 <i>Successfully completed n=101:</i> I: 31 C1: 36 C2: 34	n=7	RYGB surgery: Diabetes remission: 28/31 (90%)	C1: Usual Care: Diabetes remission: 0 p<0.0001* C2: Usual care + Exenatide: Diabetes remission: 0 p<0.0001*	Patient with type 2 diabetes, BMI >28 kg/m ² and hypertension. Study performed in China, where BMI over 28 is classified as obesity. No upper limit for BMI stated, but mean BMI ≈30.4 kg/m ² . Comparison between RYGB surgery, usual medical care and usual medical care combined with Exenatide. 12 months follow up. Primary aim: Study of change in cardiac function.	?	?	?
Petry, 2015, Brazil (data analysed in USA)	RCT	n=23 I: 12 C: 11	n=6 I: 2 C: 4	DJBm: "Complete" diabetes remission: 0 "Partial" diabetes remission: 1	Standard care: "Complete" diabetes remission: 0 n.s.* "Partial" diabetes remission: 0 n.s.*	Intervention: DJBm=duodenal-jejunal bypass surgery with minimal gastric resection Control: "Standard care" according to guidelines provided by the Federal Health Authority of Brazil Patients with type 2 diabetes and overweight or obesity. Upper limit for BMI 39,9 kg/m ² . Range according to the subject characteristics however 25.1-37.6 kg/m ² . Mean BMI; I: 29.7(1.9) vs C: 31.7(3.5) kg/m ² .	?	-	-

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:2

Outcome variable: Remission of type-2 diabetes

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Wentworth, 2014, Australia	RCT	n=51 I:25 C:26	n=3 I: 2 C: 1	Gastric banding + multidisciplinary care: Diabetes remission: 12 patients (52%)	Multidisciplinary care: Diabetes remission: 2 patients (8%) Difference in proportions between the two groups: 0.44, 95% CI 0.17-0.71; p=0.0012	Patients with type 2 diabetes and BMI 25-30 kg/m ² . Two years follow up.	+/?	+	+
Abbatini, 2012, Italy	Cohort	n=18 I:9 C:9	0	Sleeve gastrectomy: Remission of type 2 diabetes: 8/9 (88.8%)	Conventional medical treatment: Remission of type 2 diabetes: 0 of the patients. p=0.0004*	Patients with type 2 diabetes and overweight or obesity. BMI 28-35 kg/m ² . Consecutively enrolled. Matched. Laparoscopic sleeve gastrectomy compared with conventional medical therapy. Conventional medical therapy not thoroughly described. 12 months follow up.	+/?	?/-	-

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:2

Outcome variable: Remission of type-2 diabetes

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Scopinaro, 2011b, Italy	Cohort	n=68 I: 30 C: 38	n=0 ?	Biliopancreatic diversion: Diabetes resolution: 9/30 (30%).	Standard care: Diabetes resolution: 0/38 patients. p= 0.0003*	Patients with type 2 diabetes and overweight or obesity (BMI 25-35 kg/m ²). Biliopancreatic diversion vs patients matched on selected baseline characteristics from a database at a Diabetology center receiving standard care (no active medical intervention). One year follow up.	?	?/-	-
Scopinaro, 2014, Italy	Cohort	n=47 I:20 C:27	0 ?	RYGB surgery: Diabetes remission: 12 months: 5 patients (25%) 36 months: 5 patients (25%)	Standard care: Diabetes remission: 12 months: 0 patients (0%) p<0.0001* 36 months: 0 patients (0%) p<0.0001*	Patients with type 2 diabetes and BMI 30-35 kg/m ² . Twenty patients recruited for Roux-en-Y gastric bypass surgery. Twenty-seven patients matched for selected baseline characteristics and followed prospectively as a control group. Three years follow up. Controls: "Drug administration in the control group was managed by the diabetologist on a case-by-case basis according to GCP."	?	?	?

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:2

Outcome variable: Remission of type-2 diabetes

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	*	* Directness	* Study limitations	* Precision
				Intervention	Control					

Serrot, 2011, USA	Cohort	n=34 I: 17 C: 17	n=0	Roux-en-Y gastric bypass: Diabetes remission: 11/17 (65%)	Medical management: Diabetes remission: not presented (null?)	Roux-en-Y gastric bypass surgery vs medical management. Retrospective review of bariatric surgery database, including patients with type 2 diabetes and BMI <35 kg/m ² <i>at the time of surgery</i> . All patients had met the NIH criteria for obesity surgery at the time of their initial evaluation. Medical management control group from university primary care database. Group matched with intervention group for BMI.	+/-	-	-
-------------------	--------	------------------------	-----	---	---	---	-----	---	---

* p-values calculated from presented data (Fisher's exact test). I = Intervention. C = Control. BMI = Body Mass Index. n.s. = not significant. RYGB = Laparoscopic Roux-en-Y-gastric bypass. DJBm=Duodenal-jejunal Bypass surgery with minimal gastric resection. OW=Overweight. OB=Obese. GCP=Good Clinical Practice

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:3

Outcome variable: Health related quality of life (HRQoL)

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Wentworth, 2014, Australia	RCT	N= 51 I=25 C=26	3	SF-36 Physical wellbeing at 2 years, mean (95%CI): 7.7 (5.0 to 10.4) p<0.0001 SF-36 Mental wellbeing at 2 years, mean (95%CI): -0.13 (-6.8 to 6.5) n.s.	SF-36 Physical wellbeing at 2years, mean (95%CI): -1.7 (-5.3 to 1.9) SF-36 Mental wellbeing at 2 years, mean (95%CI): -0.82(-5.2 to 3.6)	I. Medical treatment +LAGB C. Medical treatment	+/?	+	+

LAGB, laparoscopic adjustable gastric band. n.s. = not significant.

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:4

Outcome variable: Glycaemic control (HbA1c)

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Liang, 2013, China	RCT	n=108 <i>Successfully completed 101</i> I: 31 C1: 36 C2: 34	n=7	RYGB: mean (SD) Baseline: 10.47 (1.17)% Follow up: 5.98 (0.3)%	C1: Usual Care: mean (SD) Baseline: 10.88 (1.40)% Follow up: 8.14 (0.27)% p<0.05 for RYGB vs usual care after 12 months C2: Usual care + Exenatide: mean (SD) Baseline: 10.52 (1.49)% Follow up: 7.10 (0.26)% p<0.05 for RYGB vs Exenatide after 12 months. (p<0.05 for RYGB or Exenatide post treatment vs pre treatment)	Patient with type 2 diabetes, BMI >28 kg/m ² and hypertension. Study performed in China, where BMI over 28 is classified as obesity. No upper limit for BMI stated, but mean BMI ≈30.4 kg/m ² . Comparison between RYGB surgery, usual medical care and usual medical care combined with Exenatide. 12 months follow up. Primary aim: Study of change in cardiac function.	?	?	?

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:4

Outcome variable: Glycaemic control (HbA1c)

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Petry, 2015, Brazil (data analyses in USA)	RCT	n=23 I: 12 C: 11	n=6 I: 2 C: 4	DJBM: mean (SD) Baseline: 8.7 (1.3)% Follow up: 7.5 (1.0)%	Standard care: mean (SD) Baseline: 8.3 (1.0)% Follow up: 7.7 (1.3)% n.s. between groups. (p<0.05 for follow up vs basal value within each group separately)	Intervention: DJBM=duodenal-jejunal bypass surgery with minimal gastric resection Control: "Standard care" according to guidelines provided by the Federal Health Authority of Brazil Patients with type 2 diabetes and overweight or obesity. Upper limit for BMI 39.9 kg/m ² . Range according to the subject characteristics however 25.1-37.6 kg/m ² . Mean BMI; I: 29.7 (1.9) vs C: 31.7 (3.5) kg/m ² .	?	-	-
Schauer, 2014, USA	RCT	n=150 RYGB: 50 Sleeve:50 Medical: 50 <i>Patients with BMI < 35 kg/m²: n=49</i>	n=13 <i>n=150</i> RYGB: 2 Sleeve: 1 Medical: 10 <i>Not presented for patients with BMI <35 kg/m².</i>	RYGB or sleeve gastrectomy + intensive medical treatment: HbA1c Baseline: 9.1% 3 years: 7.1%	Intensive medical treatment: HbA1c Baseline: 9.4 % 3 years: 8.1% p=0.008 between groups	Comparison between intensive medical treatment, combined with gastric bypass or sleeve surgery, compared to intensive medical treatment. 3 years follow up. BMI 27-43 kg/m ² included in the study. However, some data separately presented for subjects with BMI < 35 kg/m ² . In the present study only <i>results</i> from this group are included, due to the inclusion criteria of the HTA project. In the subgroup of patients with BMI <35 kg/m ² data from RYGB and sleeve gastrectomy are pooled and not <i>separately</i> presented.	+	+/?	+/?

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:4

Outcome variable: Glycaemic control (HbA1c)

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Wentworth, 2014, Australia	RCT	n=51 I:25 C:26	n=3 I: 2 C: 1	Gastric banding + multidisciplinary care: HbA1c (%): mean (SD) Baseline: 6.9 (1.2) Follow up: 6.1 (1.0) Change from baseline: -0.8% (95%CI: -1.1 to -0.5) p<0.0001 vs baseline	Multidisciplinary care: HbA1c (%): mean (SD) Baseline: 7.2 (1.1) Follow up: 7.3 (1.4) Change from baseline: 0.0% (95%CI: -1.2 to 1.4) p=0.92 vs baseline Intergroup difference at follow up: 1.2 (0.5 to 1.9); p=0.0013	Patients with type 2 diabetes and BMI 25-30 kg/m ² . 2 years follow up.	+/?	+	+
Abbatini, 2012, Italy	Cohort	n=18 I:9 C:9	n=0	Sleeve gastrectomy: (mean (SD)) HbA1c, %: Baseline: 8.1 (0.07) Follow up: 5.9 (1.7)	Conventional medical therapy: (mean (SD)) HbA1c, %: Baseline: 7.5 (1.6) Follow up: 8.2 (1.8) p<0.05 for medical treatment vs surgery at follow up (n.s. between groups at baseline)	Patients with type 2 diabetes and overweight or obesity. BMI 28-35 kg/m ² . Consecutively enrolled. Matched. Laparoscopic sleeve gastrectomy compared with conventional medical therapy. Conventional medical therapy not thoroughly described. 12 months follow up.	+/?	?/-	-

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:4

Outcome variable: Glycaemic control (HbA1c)

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Geloneze, 2012, Brazil	Cohort	n=41 I: 19 C: 22	n=5 I: 1 C: 4	Duodenal-jejunal bypass: HbA1c, %: Mean (SD) Baseline: 8.9 (1.4) Follow up: 8.0 (0.8)	Standard medical care: HbA1c, %: Mean (SD) Baseline: 8.8 (1.0) Follow up: 8.6 (0.9) p<0.05 between the two groups for HbA1c at follow up. n.s. for follow up vs baseline in both groups	Patients with type 2 diabetes and BMI 25-29.9 kg/m ² . Duodenal-jejunal bypass vs standard medical care. 12 months follow up. The non-surgical group was composed of patients who refused the surgical procedure, but matched selected baseline characteristics. Standard medical care: "Not standardized, but included pharmacological and non-pharmacological approaches according to current Brazilian guidelines."	?/-	?/-	-
Scopinaro, 2011a, Italy	Cohort	n=68 I, overweight: n=15 I, obese: n=15 C, overweight: n=18 C, obese: n=20	n=0	Biliopancreatic diversion: HbA1c, %: mean (SD) OW: Baseline: 9.1 (1.3) 12 months: 7.1 (1.1) 24 months: 6.9 (1.1) OB: Baseline: 9.5 (1.6) 12 months: 5.9 (0.6) 24 months : 5.9 (0.9)	Standard care: HbA1c, %: mean (SD) OW: Baseline: 8.1 (0.8) 12 months: 7.6 (0.5) 24 months: 7.4 (0.3) OB: Baseline: 8.4 (0.7) 12 months: 7.8 (0.8) 24 months: 7.6 (0.4)	Patients with type 2 diabetes and overweight (BMI 25-30 kg/m ²) or mild obesity (BMI 30-35 kg/m ²). Biliopancreatic diversion vs patients matched on selected baseline characteristics from a database at a Diabetology center receiving standard care (no active medical intervention). Two years follow up. The primary focus of the publication is comparison between the results of	?	?	-

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:4

Outcome variable: Glycaemic control (HbA1c)

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	*	* Directness	* Study limitations	* Precision
				Intervention	Control					
				p<0.05 from baseline to 12 and 24 months follow up in the group undergoing biliopancreatic diversion.	p<0.01 between the two groups at baseline. No statistics presented regarding differences between intervention and control at follow up. p<0.01 from baseline to 12 and 24 months follow up in the standard care group.	surgery in overweight compared to mildly obese patients.				
Scopinaro, 2011b, Italy	Cohort	n=68 I: 30 C: 38	n=0 (?)	Biliopancreatic diversion: HbA1c, %: mean (SD) Baseline: 9.3 (1.5) 12 months: 6.5 (0.8) p<0.05 from baseline to 12 and 24 months follow up in the group undergoing biliopancreatic diversion.	Standard care: HbA1c, %: mean (SD) Baseline: 8.3 (0.8) 12 months: 7.7 (0.7) p<0.01 between the two groups at baseline. No statistics presented regarding differences between intervention and control at follow up. p<0.01 from baseline to 12 months follow up in the standard care group.	Patients with type 2 diabetes and overweight or obesity (BMI 25-35 kg/m ²). Biliopancreatic diversion vs patients matched on selected baseline characteristics from a database at a Diabetology center receiving standard care (no active medical intervention). One year follow up. NB: same study as Scopinaro 2011b Italy (Obes surg) but different presentation of results.	?	?/-	-	

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:4

Outcome variable: Glycaemic control (HbA1c)

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Scopinaro, 2014, Italy	Cohort	n=47 I:20 C:27	n=0 (?)	RYGB surgery: HbA1c, %: mean (SD) Baseline: 9.5 (1.8) 12 months: 7.1 (1.1) 36 months: 7.0 (1.4)	Standard care: HbA1c, %: mean (SD) Baseline: 9.3 (1.4) 12 months: 7.6 (0.5) 36 months: 7.7 (0.9) n.s. for comparison between the two groups. p<0.01 for baseline to 12 and 36 months follow up in both groups.	Patients with type 2 diabetes and BMI 30-35 kg/m ² . Twenty patients recruited for Roux-en-Y gastric bypass surgery. Twenty-seven patients matched for selected baseline characteristics and followed prospectively as a control group. Three years follow up. Controls: "Drug administration in the control group was managed by the diabetologist on a case-by-case basis according to GCP."	?	?	?
Serrot, 2011, USA	Cohort	n=34 I: 17 C: 17	n=0	RYGB: HbA1c, %: median (IQR) Baseline: 8.2 (2.0) 12 months: 6.1 (2.7) p<0.001 for baseline to follow up in surgery group.	Medical management: HbA1c, %: Median (IQR) Baseline: 7.0 (0.7) 12 months: 7.1 (1.8) p=0.04 between the two groups at baseline. n.s. from baseline to follow up in control group.	Roux-en-Y gastric bypass surgery vs medical management. Retrospective review of bariatric surgery database, including patients with type 2 diabetes and BMI <35 kg/m ² at the time of surgery. All patients had met the NIH criteria for obesity surgery at the time of their initial evaluation. Medical management control group from university primary care database. Group matched with intervention group for BMI.	+/-	-	-

I = Intervention. C = Control. BMI = Body Mass Index. n.s. = not significant. RYGB = Laparoscopic Roux-en-Y-gastric bypass. DJBm=Duodenal-jejunal Bypass surgery with minimal gastric resection. OW=Overweight. OB=Obese. HbA1c = Glycated Haemoglobin (Measured to evaluate the average plasma glucose concentration during the last 6-8 weeks.) IQR = Interquartile range.

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:5

Outcome variable: Other metabolic risk factors (i.e. dyslipidemia, hypertension, sleep apnea, inflammatory mediators and adiponectin)

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Liang, 2013, China	RCT	n=108 C=36 I1=34 I2=31	7	Tot. chol.: I2 -34.5% TG: I2 -52.8% LDL-C: I2 -48.7% HDL-C: I2 +36.0% hs-CRP: I2 -53.1% TNF-α: I2 -36.4% Adiponectin: I2 +113% LVMI: I2 -5.4%	C: No effects Tot. chol.: I1 -18.6% TG: I1 -21.6% LDL-C: I1 -28.0%, HDL-C: I1 +13.3% hs-CRP: I1 -35.4% TNF-α: I1 -12.5% Adiponectin: I1 +32.3%,	C: Usual care I1: Usual care + Exenatide I2: LRYGB BMI ≈30.4±1.45 kg/m ² (mean±SD).	?	?	?
Wentworth, 2014, Australia	RCT	n=51 I=25 C=26	3	Tot chol.: +2.2% (NS) TG: -35.3% HDL-C: +20.8% (NS) LDL-C: +3.8% (NS)	C: No effects	I: Multidisciplinary care + LAGB C: Multidisciplinary care only BMI=25-30 kg/m ²	+/?	+	+
Abbatini, 2012, Italy	Cohort (matched)	n=18 I=9 C=9	0	Resolution of hypertension: 8/9 patients (88.9%). Dyslipidemia corrected: 9/9 patients (100%). OSAS improvement: 1/1 patients (100%).	C: No effects	I: LSG C: Medical treatment only	+/?	?/-	-
Geloneze, 2012, Brazil	Cohort	n=41 I=18 C=18	5	No effect hyperlipidemia, , hypertension, hsCRP,	C: No effects	I: OJOB C: Medical therapy	?/-	?/-	-

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:5

Outcome variable: Other metabolic risk factors (i.e. dyslipidemia, hypertension, sleep apnea, inflammatory mediators and adiponectin)

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Scopinaro, 2011a, Italy	Cohort	n=68 I1=15 I2=15 C1=20 C2=18	-	Hypertension I1: -8/15 patients (-53.3%). Tot. chol.: I1 -17.9% Tot. chol.: I2 -23.2% Hypercholesterolemia I1: -6/15 patients (-43%). Hypercholesterolemia I2: -8/15 patients (-53%). HDL-C I1: +4.4% HDL-C I2: -22.4% Hypertriglyceridemia I1: +3/15 patients (+20%) Hypertriglyceridemia I2: +8/15 patients (+53%)	TG C1: -15.0% TG C2: -17.3% Antihyperlipemic therapy C1: +5/19 patients (+28.9%) Antihyperlipemic therapy C2: +2/18 patients (+11.0%)	I1: BPD (BMI 30.0-34.9) I2: BPD (BMI 25.0-29.9) C1: Medical therapy (BMI 30.0-34.9) C2: Medical therapy (BMI 25.0-29.9)	?	?	-
Scopinaro, 2011b, Italy	Cohort	n=68 I=30 C=38	-	Hypertension: -12/30 patients (-40%). Hypercholesterolemia: -14/30 patients (-47%). Tot. chol.: -22.6% Hypertriglyceridemia: +8/30 patients (+27%). HDL-C: -6.4%	C: No effects	I: BPD C: Medical therapy	?	?/-	-
Scopinaro, 2014, Italy	Cohort	n=47 I=20 C=27	0	Hypertension: -7/20 patients (-35%). TG: -50.2% Hyper-TG: -10/20 patients (-50.0%) Tot. chol.: -12.1% Hyper-chol.: -8/20 patients (-40%). HDL-C: +26.3%	TG: -38.2% Proportion hyper-TG: not given Tot. chol.: -21.1% Antihyperlipemic therapy: +55% HDL-C: +19.3% (n.s.)	I: LRYGB C: Medical therapy	?	?	?

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:5

* + No or minor problems
? Some problems
- Major problems

Outcome variable: Other metabolic risk factors (i.e. dyslipidemia, hypertension, sleep apnea, inflammatory mediators and adiponectin)

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				

Serrot, 2011, USA	Cohort	n=34 I=17 C=17	-	Antihypertensive medication: -35% (compared with C). Antihyperlipemic medication: -35% (compared with C).	C: No effects	I: LRYGB C: Non-surgical Care (NSC).	+/-	-	-
-------------------	--------	----------------------	---	--	---------------	---	-----	---	---

LRYGB=Laparoscopic Roux-en-Y Gastric bypass, LDJB=Laparoscopic Duodenal-jejunal Bypass + mini gastrectomy, LSG=Laparoscopic sleeve gastrectomy, LAGB=Laparoscopic Adjustable Gastric Band, ODJB=Open Duodenal Jejunal Bypass, BPD=Biliopancreatic diversion with duodenal switch.

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:6

Outcome variable: BMI (body weight)

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results		Comments	*	*	*
				Intervention	Control				
Liang, 2013, China	RCT	n=108 I1=31 I2=34 C=36	7	Preop =>1y data; mean (SD) 30.48 (0.93)=> 24.51(0.91) (-20%) Intergroup difference at one year p<0.01	Baseline =>1y data;mean (SD) 30.94 ±1.96=>30.38±1.66 (-1.7%)	I1. RYGB I2. Exenatide + Usual care C. Usual care	?	?	?
Petry, 2015, Brazil	RCT	n=23 I=12 C=11	6	1y follow-up mean (SD) B.w. change: -10.4% (4.3) Intergroup difference in absolute terms at 1y (p<0.05)	1y follow-up: mean (SD) B.w. change: <1%	Note: presents body weight (BMI only at inclusion) I. lap DJB (+ mini gastrectomy) C. Standard care	?	-	-
Schauer, 2014, USA	RCT	n=150 I1=50 I2=50 C=50	13	3y follow-up: BMI mean change -7% Intergroup difference at 3y: p<0.001 (surgery = I1+I2)	3y follow-up: BMI mean change -0.5%	Inclusion BMI<35 only graphically presented (Fig S2) I1 LSG+medicine I2 lapRYGB + medicine C. Medicine only	+	+/?	+/?
Wentworth, 2014, Australia	RCT	n= 51 I=25 C=26	3	2y follow-up: BMI change, mean (95%CI) -4.1 (-5.1 to -3.2) (-14%) Intergroup difference: p<0.0001	2y follow-up: BMI change, mean (95%CI) -0.5 (-1.3 to 0.3) (-2%)	I. Medicine+LAGB C. Medicine	+/+	+	+
Abbatini, 2012, Italy	Cohort (matched)	n=18 I=9 C=9	0	Preop =>1y data; mean (SD) 32.7 (3.2) =>21.1±3.6 (-35%) Intergroup difference at 1y: p<0.05	Baseline =>1y data ;mean (SD) 32.9 (2.0) =>31.7 (1.9) (-3.6%)	I. LSG C. Medicine	+/?	?/-	-

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:6

Outcome variable: BMI (body weight)

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With draws - dropouts	Results		Comments	*	* Directness	* Study limitations	* Precision
				Intervention	Control					
Geloneze, 2012, Brazil	Cohort	n=41 I=18 C=18	5	Preop =>1y data; mean (SD) 26.1 (1.7) => 26.4(2.6) (+1%)	Baseline =>1y data; mean (SD) 26.3(1.2) => 25.9(1.9) (-1.5%)	I. Open DJB C. Medicine	?/-	?/-	-	
Scopinaro, 2011a, Italy	Cohort	n=68 I1=15 I2=15 C1=20 C2=18	-	2y data; mean (SD) I1: 33.1 (1.5) => 27.4 (2.3) I2: 28.1 (1.4) => 24.6 (1.8) (-14%)	Baseline =>2y data; mean (SD) C1: 32.9 (1.8) => 33.1 (32.1) C2: 27.1 (2.1) =>26.9(2.0) (±0%) p-value not stated	I1. BPD (BMI 30-35) I2. BPD (BMI 25-30) C1. Medicine (BMI 30-35) C2. Medicine(BMI 25-30)	?	?/-	-	
Scopinaro, 2011b, Italy	Cohort	n=68 I=30 C=38	-	Preop =>1y data; mean (SD) 30.6 (2.9) => 25.3 (2.3) (-23%)	Baseline =>1y data; mean (SD) 30.2 (3.5) => 30.2 (3.6) (0%) p-value not stated	I. BPD C. Medicine	?	?	-	
Scopinaro, 2014, Italy	Cohort	n=47 I=20 C=27	0	Preop =>3y data: mean (SD) 32.9 (1.5) => 26.0 (2.2) (-21%)	Baseline =>3y data: mean (SD) 33.0 (1.6) =>32.6 (1.4) (-1.1%) p-value not stated	I. lapRYGB C. Medicine	?	?	?	
Serrot, 2011, USA	Cohort	n=34 I=17 C=34	-	Preop =>1y data; mean(SD) 34.6 (0.8) => 25.8 (2.5) (-25%) Intergroup difference p<0.001	Baseline =>1y data; mean (SD) 34.0±31.8 => 34.3 (2.1) (+1%)	I. lapRYGB C. Medicine	?/-	-	-	

Percentage-change within brackets are calculated from the presented mean values. B.w., body weight; BMI, body mass index, CI, confidence interval; SD, standard deviation; lapRYGB, laparoscopic Roux-en-Y gastric bypass; LAGB, laparoscopic adjustable gastric band; lapDJB, laparoscopic duodenal-jejunal bypass; BPD, biliary-pancreatic diversion, LSG, laparoscopic sleeve gastrectomy.

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:7

Outcome variable: Fasting plasma glucose (fP-glucose)

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With drawsals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Petry, 2015, Brazil (data analysed in USA)	RCT	n=23 I: 12 C: 11	n=6 I: 2 C: 4	DJBm: fP-glucose (mg/dl) (mean (SD)) Baseline: 203 (64) Follow up: 146 (26) Intergroup difference n.s. p<0.05, intragroup difference	Standard care: fP-glucose (mg/dl) (mean (SD)) Baseline: 198 (59) Follow up: 157 (50) p<0.05 intragroup difference	Intervention: DJBm=duodenal-jejunal bypass surgery with minimal gastric resection Control: "Standard care" according to guidelines provided by the Federal Health Authority of Brazil Patients with type 2 diabetes and overweight or obesity. Upper limit for BMI 39,9 kg/m ² . Range according to the subject characteristics however 25.1-37.6 kg/m ² . Mean BMI; I: 29.7 (1.9) vs C: 31.7 (3.5) kg/m ² .	?	-	-
Wentworth, 2014, Australia	RCT	n=51 I:25 C:26	n=3 I: 2 C: 1	Gastric banding + multidisciplinary care: fP-Glucose (mmol/L) (mean(SD)) Baseline: 7.4 (2.1) Follow up: 6.5 (1.0) Intergroup difference at follow up: 1.9 (0.6 to 3.1); p-value 0.0038 fP-Glucose, change from baseline (95%CI): -1.0 (-1.7 to -0.3)	Multidisciplinary care: fP-Glucose (mmol/L) (mean (SD)) Baseline: 8.2 (2.3) Follow up: 8.4 (2.6) fP-Glucose, change from baseline (95%CI): +0.1 (-1.2 to 1.4)	Patients with type 2 diabetes and BMI 25-30 kg/m ² . 2 years follow up.	+/?	+	+

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:7

Outcome variable: Fasting plasma glucose (fP-glucose)

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With draws - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Abbatini, 2012, Italy	Cohort	n=18 I:9 C:9	0	Sleeve gastrectomy: mean(SD): fP-Glucose, mg/dL: Baseline: 139.5 (3.5) Follow up: 82.6 (2.1)	Conventional medical therapy mean (SD): fP-Glucose, mg/dL: Baseline: 148.7 (40.1) Follow up: 164 (63.5) (n.s. between groups at baseline) p<0.05 intergroup difference at follow up	Patients with type 2 diabetes and overweight or obesity. BMI 28-35 kg/m ² . Consecutively enrolled. Matched. Laparoscopic sleeve gastrectomy compared with conventional medical therapy. Conventional medical therapy not thoroughly described. 12 months follow up.	+/?	?/-	-
Geloneze, 2012, Brazil	Cohort	n=41 I: 19 C: 22	n=5 I: 1 C: 4	Duodenal-jejunal bypass: fP-Glucose (mmol/L): (mean (SD)) Baseline: 9.9 (3.5) Follow up: 8.3 (2.5)	Standard medical care: fP-Glucose (mmol/L): (mean (SD)) Baseline: 9.7 (2.8) Follow up: 9.1 (2.6) p<0.05 intergroup difference at follow up. p<0.05 at follow up vs baseline in both groups.	Patients with type 2 diabetes and BMI 25-29.9 kg/m ² . Duodenal-jejunal bypass vs standard medical care. 12 months follow up. The non-surgical group was composed of patients who refused the surgical procedure, but matched selected baseline characteristics. Standard medical care: "Not standardized, but included pharmacological and non-pharmacological approaches according to current Brazilian guidelines:"	?/-	?/-	-

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:7

Outcome variable: Fasting plasma glucose (fP-glucose)

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With draws - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Scopinaro, 2011b, Italy	Cohort	n=68 I: 30 C: 38	n=0 (?)	Biliopancreatic diversion: fP-Glucose, mg/dL: (mean (SD)) Baseline: 220 (69) 12 months: 149 (41) p<0.05 from baseline to follow up in the group undergoing biliopancreatic diversion.	Standard care: fP-Glucose, mg/dL: (mean (SD)) Baseline: 171 (38) 12 months: 151 (28) p<0.01 between the two groups at baseline. No statistics presented regarding differences between intervention and control at follow up. p<0.01 from baseline to follow up in the standard care group.	Patients with type 2 diabetes and overweight or obesity (BMI 25-35 kg/m ²). Biliopancreatic diversion vs patients matched on selected baseline characteristics from a database at a Diabetology center receiving standard care (no active medical intervention). One year follow up. NB. Same study as Scopinaro 2011a Italy, but different presentation of results.	?	?/-	-

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:7

Outcome variable: Fasting plasma glucose (fP-glucose)

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With draws - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Scopinaro, 2014, Italy	Cohort	n=47 I:20 C:27	0 ?	RYGB surgery: fP-Glucose (mg/dl): (mean (SD)) Baseline: 207 (58) 12 months: 148 (8) 36 months: 140 (49) p<0.01 for follow up vs baseline at 12 and 36 months in surgical group.	Standard care: fP-Glucose (mg/dl): (mean (SD)) Baseline: 187 (42) 12 months: 162 (28) 36 months: 158 (27) n.s. for comparisons between the two groups. p<0.05 for follow up vs baseline at 12 and 36 months in controls.	Patients with type 2 diabetes and BMI 30-35 kg/m ² . Twenty patients recruited for Roux-en-Y gastric bypass surgery. Twenty-seven patients matched for selected baseline characteristics and followed prospectively as a control group. Three years follow up. Controls: "Drug administration in the control group was managed by the diabetologist on a case-by-case basis according to GCP."	?	?	?

HOMA-IR = Homeostatic Model Assessment of insulin resistance. BMI = Body Mass Index. n.s. = not significant. RYGB = Laparoscopic Roux-en-Y-gastric bypass. DJBm=Duodenal-jejunal Bypass surgery with minimal gastric resection. OW=Overweight. OB=Obese. fP-Glucose = Fasting Plasma Glucose concentration. fS-Glucose = Fasting Serum Glucose concentration.

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:8

Outcome variable: Medication (medication score or average number of medications)

* + No or minor problems
 ? Some problems
 - Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Petry, 2015, Brazil (data analysed in USA)	RCT	n=23 I: 12 C: 11	n=6 I: 2 C: 4	DJbM: Medication score: Baseline: 1.0 Follow-up: 0.8 <i>(Data extracted from a graphical presentation.)</i>	Standard care: Medication score: Baseline: 0.8 Follow-up: 1.4 <i>(Data extracted from a graphical presentation.)</i> “There was a significant interaction between time and group (p<0.01) in the composite score for the use of diabetes medications” with increased score in standard care group and decreased score in the surgery group. However, not possible to detect a statistically significant increase in medications in the standard care group alone or a statistically significant decrease in the surgery group alone.	Intervention: DJbM=duodenal-jejunal bypass surgery with minimal gastric resection Control: “Standard care” according to guidelines provided by the Federal Health Authority of Brazil Patients with type 2 diabetes and overweight or obesity. Upper limit for BMI 39.9 kg/m ² . Range according to the subject characteristics however 25.1-37.6 kg/m ² . Mean BMI; I: 29.7 (1.9) vs C: 31.7 (3.5) kg/m ² .	?	-	-

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:8

Outcome variable: Medication (medication score or average number of medications)

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results		Comments	*	* Directness	* Study limitations	* Precision
				Intervention	Control					
Schauer, 2014, USA	RCT	n=150 RYGB: 50 Sleeve: 50 Medical: 0	n=13 (n=150) RYGB: 2 Sleeve: 1 Medical: 10	RYGB surgery or sleeve gastrectomy + intensive medical treatment Mean numbers of diabetes medications; ≈1.1 (result estimated from a graphical presentation)	Intensive medical treatment ≈2.7 (result estimated from a graphical presentation) p<0.01	Comparison between intensive medical treatment, combined with gastric bypass or sleeve surgery, compared with intensive medical treatment. 3 years follow up. BMI 27-43 kg/m ² included in the study. However, some data separately presented for subjects with BMI < 35 kg/m ² . In the present study only <i>results</i> from this group are included, due to the inclusion criteria of the HTA project. In the subgroup of patients with BMI <35 kg/m ² data from RYGB and sleeve gastrectomy are pooled and not <i>separately</i> presented.	+	+/?	+/?	
Scopinaro, 2011b, Italy	Cohort	n=68 I: 30 C: 38	n=0 ?	Biliopancreatic diversion: 19/30 (63%) of the patients never required any antidiabetic medication during 12 months follow up. (p-value not stated)	Standard care: All (100%) patients required antidiabetic medication 12 months after enrolment in the study.	Patients with type 2 diabetes and overweight or obesity (BMI 25-35 kg/m ²). Biliopancreatic diversion vs patients matched on selected baseline characteristics from a database at a Diabetology center receiving standard care (no active medical intervention). One year follow up.	?	?/-	-	

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:8

Outcome variable: Medication (medication score or average number of medications)

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With draws - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Serot, 2011, USA	Cohort	n=34 I: 17 C: 17	n=0	Roux-en-Y gastric bypass: “Medication score”, diabetes medications: 14	Medical management: “Medication score”, diabetes medications: 9 n.s. between intervention and control group (p=0.25)	Roux-en-Y gastric bypass surgery vs medical management. Retrospective review of bariatric surgery database, including patients with type 2 diabetes and BMI <35 kg/m ² at the time of surgery. All patients had met the NIH criteria for obesity surgery at the time of their initial evaluation. Medical management control group from university primary care database. Group matched with intervention group for BMI. Medication score = No antidiabetics: 0 p. Metformin: 1 p. An additional point was assigned for use of each additional oral antidiabetic agent or exenatide. Insulin=2 points added.	+/-	-	-

I = Intervention. C = Control. BMI = Body Mass Index. n.s. = not significant. RYGB = Laparoscopic Roux-en-Y-gastric bypass. DJBm=Duodenal-Jejunal Bypass surgery with minimal gastric resection. OW=Overweight. OB=Obese. IQR = Interquartile range.

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:9

Outcome variable: Complications

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With draws - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Liang, 2013, China	RCT	n=108 C=36 I1=34 I2=31	7	No serious AE. Nausea I2 = 16% Local inflammation around drainage port I2 = 19%	No serious AE. Vomiting C = 8% Vomiting I1 = 38%	C=Usual care I1=Usual care + Exenatide I2=LRYGB BMI ≈30.4±1.45 kg/m ² (mean±SD)	?	?	?
Petry, 2015, Brazil	RCT	n=23 I=12 C=11	6	One anastomotic leak, surgical repair (8%)	No AE.	I=LDJB C=Standard Medical Care	?	-	-
Schauer, 2014, USA	RCT	n=150 I1=50 I2=50 C=50	13	Surgical complications, reoperation first 12 mo = 4%	Excessive weight gain (>5%) = 7/43 patients (16.3%)	C. Medical therapy I1=LSG+medical therapy I2 LRYGB+ medical therapy	+	+/?	+/?
Wentworth, 2014, Australia	RCT	n= 51 I=25 C=26	3	Revisional surgery = 1 (4%) Food intake intolerance leading to band adjustment = 4 (17%). Postoperative cholecystectomy = 1 (4%)	Retinal photocoagulation = 2 (8%) Eosinophilic fascitis (Atorvastatin) = 1 (4%)	I. Medical therapy+LAGB C. Medical therapy	+/?	+	+
Abbatini, 2012, Italy	Cohort (matched)	n=18 I=9 C=9	0	"No major complications."		I. LSG C. Medical therapy	+/?	?/-	-
Geloneze, 2012, Brazil	Cohort	n=41 I=18 C=18	5	Early postop nausea = 10/18 pat (55.6%) Hypoglycemic events = 3 pats (before insulin withdrawal, 16.7%)	Hypoglycemic events = 12/18 pat (66.7%)	I. ODJB C. Medical therapy	?/-	?/-	-

Project: Bariatric surgery for diabetes control in adults with BMI <35 kg/m²

Appendix 4:9

Outcome variable: Complications

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With draws - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Scopinaro, 2011a; 2011b, Italy	Cohort	n=68 I=30 C=38	-	Open surgery in 16 cases, laparoscopic in 14 Intraperitoneal bleeding = 1/30 (3.3%) Early gastroplegia (within <2 weeks) = 4/30 (13.3%)		I. BPD C. Medical therapy	?	?/-	-
Scopinaro, 2014, Italy	Cohort	n=47 I=20 C=27	0	Intraperitoneal bleeding = 1/20 (5%) Gastrointestinal bleeding = 1/20 (5%) Stomal ulcer bleeding=1/20 (5%) Intestinal obstruction/internal herniation = 1/20 (5%)		I. LRYGB C. Medical therapy	?	?	?
Serrot, 2011, USA	Cohort	n=34 I=17 C=17	-	Internal herniations = 2/17 patients (11.8%) Marginal ulcers = 2/17 patients (11.8%)		I. LRYGBP C. Non-surgical care (NSC).	+/-	-	-

AE= adverse events, LRYGB=Laparoscopic Roux-en-Y Gastric bypass, LDJB=Laparoscopic Duodenal-jejunal Bypass + mini gastrectomy, LSG=Laparoscopic sleeve gastrectomy, LAGB=Laparoscopic Adjustable Gastric Band, ODJB=Open Duodenal Jejunal Bypass, BPD=Biliopancreatic diversion with duodenal switch

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE ⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕○)
Low quality of evidence	= (GRADE ⊕⊕○○)
Very low quality of evidence	= (GRADE ⊕○○○)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh, Professor, MD.
Head of HTA-centrum

