Canadian Agency for Drugs and Technologies in Health

RAPID RESPONSE REPORT: SUMMARY WITH CRITICAL APPRAISAL

TITLE: **Bariatric Surgery for the Long-Term Treatment of Obesity: A Review of the Clinical Effectiveness and Cost-Effectiveness**

DATE: 20 July 2016

CONTEXT AND POLICY ISSUES

Obesity is defined as a body mass index (BMI) of ≥ 30 kg/m^2, and is further classified into class I (BMI 30.0 to 34.9 kg/m^2), class II (BMI 35.0 to 39.9 kg/m^2), and class III obesity (BMI ≥ 40.0 kg/m^2), with an increase in morbidity associated with increasing class of obesity.[1] As of 2011, 18.3% of adult Canadians were obese, which represented a 200% increase from 1985.[2] Among the 18.3%, 71.6% were categorized as having class I obesity, 19.7% had class II obesity, and 8.7% had class III obesity.[2]

Obesity is associated with considerable morbidity, including hypertension, dyslipidemia, type 2 diabetes, cardiovascular disease, cancer, and osteoarthritis.[3] The increased prevalence of comorbidities associated with obesity results in a reduction in life expectancy in those who are obese compared to individuals with a BMI of 18.5 to 24.9 kg/m^2.[3]

There are a number of bariatric surgical procedures currently available, and the most commonly performed procedures are gastric bypass (GBP), sleeve gastrectomy (SG), laparoscopic adjustable gastric banding (LAGB), vertical banded gastroplasty (stomach stapling), and biliopancreatic diversion.[4,5] A 2014 CADTH Rapid Response review[6] compared the clinical and cost-effectiveness of roux-en-y gastric bypass (RYGB), SG and LAGB, and found that RYGB was associated with a greater weight reduction relative to LAGB, but was also associated with a higher risk for procedural adverse events. SG appeared to be more effective than LAGB but less effective than RYGB for weight loss, and had a reduced risk for complications relative to RYGB and a higher risk for complications relative to LABG, but evidence was conflicting. Economic evaluations of RYGB and LAGB were conducted in two cost studies, with RYGB dominating LAGB in one analysis, though the generalizability of these findings to a Canadian context is unclear. The review did not identify any evidence-based guidelines recommending specific surgical procedures.

Despite bariatric surgery having been shown to be more effective than non-surgical interventions such as medications or lifestyle changes in a number of systematic reviews of clinical trials with relatively short-term follow-up,[7,8] its long-term effectiveness is unclear. There is an increasing number of revisionary surgery (repeat surgery) that are due to undesirable results of the primary bariatric procedures, with the main cause being inadequate weight loss.[9,10]

This Rapid Response report aims to review the comparative long-term (at least five years) clinical and cost-effectiveness of bariatric surgery for the treatment of class II and class III morbid obesity.

RESEARCH QUESTIONS

1. What is the long-term clinical effectiveness of bariatric surgery for the treatment of obesity and morbid obesity?

2. What is the long-term cost-effectiveness of bariatric surgery for the treatment of obesity and morbid obesity?

KEY FINDINGS

At five years follow-up, bariatric surgeries lead to a statistically significant reduction in weight, waist circumference, and body mass index (BMI) as compared to medical treatment in patients with morbid obesity. Evidence from cost evaluation studies showed that bariatric surgery is more cost-effective than conventional treatment in patients with morbid obesity over a life time horizon. Despite higher inpatient costs leading to higher total healthcare costs at 15 years, there was no difference in total healthcare costs in the subgroup of patients with diabetes, with savings mainly driven in reduced costs of diabetes drugs.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including MEDLINE via OVID, PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. This report is an extension of a literature search conducted in March 2014 for a previous CADTH report. The current search was limited to English language documents published between March 25, 2014 and June 21, 2016.The search was also limited to English language documents.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and examined the full-text publications for the final article selection. Selection criteria are outlined in Table 1.

Table 1: Selection Criteria	
Population	Adults and children with a BMI ≥35 with severe comorbidities Adults and children with a BMI ≥40 with or without comorbidities
Intervention	Any type of bariatric surgery
Comparator	Non-surgical treatment Other surgery types (one modality of bariatric surgery compared with another modality)
Outcomes	Long term weight loss (5 years and more); Rates of repeat bariatric surgery after 5 years, Rates of qualification for repeat bariatric surgery after 5 years Cost-effectiveness (at least 5 years)
Study Designs	Health technology assessments (HTA), systematic reviews (SR), meta-analyses (MA), randomized controlled trials (RCTs), non-RCTs, economic evaluations.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1, if they were published prior to March 2014, if they were duplicate publications of the same study, or if they were referenced in a selected systematic review.

Critical Appraisal of Individual Studies

The quality of the included clinical trials, and cost evaluation was assessed using the Downs and Black[11] and Drummond[12] checklists, respectively. Numeric scores were not calculated. Instead, the strengths and limitations of the study are summarized and presented narratively.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 645 citations. After screening of abstracts from the literature search and from other sources, eight potentially relevant studies were selected for full-text review. Four studies were included in the review. The PRISMA flowchart in Appendix 1 details the process of the study selection.

Summary of Study Characteristics

A detailed summary on the design, population, interventions, comparators and outcomes of the included studies is provided in Appendix 2.

An open-label RCT assigned 60 obese patients (BMI ≥35 kg/m^2) with type 2 diabetes to receive either conventional treatment only or bariatric surgery (Roux-en-Y gastric bypass or biliopancreatic diversion). 53 patients completed five years follow-up. Control of diabetes,

reduction in weight, waist circumference, and BMI were compared between the two groups at five years follow-up.[13]

A cost study in Sweden examined the cost savings for the treatment of 4030 obese patients with different baseline fasting blood glucose levels undergoing different types of bariatric surgeries (mean age 41; mean BMI 42.7 in men, and 41.2 in women) compared to conventional treatment (ranging from advanced lifestyle modification to no treatment) over 15 years. Drug costs, inpatient and outpatient costs, and total health care costs were reported in 2013 US dollars.[14]
An economic evaluation study in Sweden evaluated the cost-utility for obese patients undergoing different types of bariatric surgeries (mean age 41; mean BMI 42.8) compared to conventional treatment using Markov modeling with a life time horizon. The model functions by predicting the risk of cardiovascular events, type 2 diabetes, and complications of surgery. Direct medical costs of bariatric surgery and medical treatment were reported in 2012 Euros (€).[15]

A cost evaluation study in Spain assessed the cost-utility for severely obese patients undergoing gastric bypass (aged 18-55; mean BMI 50.7) compared to conventional treatment using a discrete-event simulation model with various time horizons. The model assumes that all patients may develop type 2 diabetes. Direct medical costs of bariatric surgery and medical treatment were reported in 2012 €.[16]

Summary of Critical Appraisal

The included clinical trial[13] is an open label RCT, with the hypothesis, method of selection of participants from the source population and representation, method of randomization, main outcomes, interventions, patient characteristics, and main findings clearly described. Estimates of random variability and actual probability values were provided and losses to follow-up were described. The study had sufficient power to detect a clinically important effect. The patients were not blinded to the intervention, but since patients undergoing surgery had to sign informed consent and be aware of the specific risks of procedures, this is a limitation that is inherent to the nature of the intervention.

The cost study[14] had outcomes and costs assessed and compared appropriately, all the important and relevant outcomes and costs for each alternative identified. The presentation and discussion of study results include all issues of concern to users. There was no economic evaluation, incremental analysis, or sensitivity analysis performed.

The economic evaluations[15,16] are likely to be usable, outcomes and costs were assessed and compared appropriately; all the important and relevant outcomes and costs for each alternative were identified; outcomes and costs were measured accurately in appropriate units prior to evaluation; outcomes and costs were valued credibly; outcomes and costs were adjusted for different times at which they occurred. An incremental analysis of the outcomes and costs of alternatives and a sensitivity analysis were performed. The presentation and discussion of study results include all issues of concern to users. The economic evaluations did not base the clinical outcomes on well-designed clinical studies. The economic models had to assume the risk of long-term complications of obesity such as cardiovascular events and type 2 diabetes.

The generalizability of the results of the economic studies to a Canadian context may be limited since costs data used Swedish[14,15] or Spanish[16] sources.

Details of the strengths and limitations of the included studies are summarized in Appendix 3.

Summary of Findings

Main findings of included studies are summarized in detail in Appendix 4.

1. What is the long-term clinical effectiveness of bariatric surgery for the treatment of obesity and morbid obesity?

An open-label RCT assigned 60 obese patients (BMI ≥35 kg/m^2) with type 2 diabetes to receive either conventional treatment only or bariatric surgery (Roux-en-Y gastric bypass or biliopancreatic diversion).[13] In all groups, diet, life style modification and dosage of insulin were optimized on an individual basis with the aim to reach adequate glycaemic control (HbA_{1c} <7.0%). At five years of follow-up, both surgical procedures lead to a statistically significant reduction in weight, waist circumference and BMI, and better control of diabetes, as compared to medical treatment.

At five years, the mean patient weight (kg) was 127.1, 90.3 and 92.8 in only medically treated, gastric bypass, and biliopancreatic diversion groups, respectively. Mean waist circumference (cm) was 113.9, 101.5 and 102.4 in only medically treated, gastric bypass and biliopancreatic diversion groups, respectively. Mean BMI (kg/m^2) was 42.1, 31.3 and 30.3 in only medically treated, gastric bypass and biliopancreatic diversion groups, respectively. The differences in all outcomes between medical treatment and surgery were statistically significant. Details on diabetes control are in presented in Appendix 4. The authors concluded that surgery is more effective than medical treatment for the long-term control of obese patients with type 2 diabetes.

2. What is the long-term cost-effectiveness of bariatric surgery for the treatment of obesity and morbid obesity?

In general, data from cost studies showed that bariatric surgery is more cost-effective than conventional treatment in patients with morbid obesity over a life time horizon, despite the fact that surgery may generate additional costs in the first 15 years. Despite higher inpatient costs at 15 years, there was no difference in total health care costs in the subgroup of patients with diabetes, with savings mainly driven in reduced costs of diabetes drugs.

A cost study in Sweden examined the cost savings for the treatment of obese patients with different baseline glucose status undergoing different types of bariatric surgeries (mean age 41; mean BMI ≥ 42.7 in men, and ≥ 41.2 in women) compared to conventional treatment over 15 years.[14] Drug costs, inpatient and outpatient costs, and total health care costs were reported in 2013 US dollars.

Drug costs did not differ between the surgery and conventional treatment group in patients with euglycaemia, but were lower in the surgery group in the prediabetes (-$3,329) and diabetes group (-$5,487). Inpatient costs were higher in the surgery group for all 3 diabetes statuses than in the conventional treatment group (euglycaemia group +$22,931, prediabetes group +$27,152, and diabetes group +$18 697). There was no difference in outpatient costs regardless of diabetes status. Total health-care costs were higher in the surgery group in the euglycaemic (+$22 390) and prediabetes (+$26 292) groups than in the conventional treatment group; there was no difference between treatment groups in patients with diabetes.

An economic evaluation study in Sweden evaluated the cost-utility for obese patients undergoing different types of bariatric surgeries (mean age 41; mean BMI 42.8) compared to conventional treatment using Markov modeling with a life time horizon.[15] Costs were direct medical costs of bariatric surgery and medical treatment and reported in 2012 €.

Over a lifetime horizon, surgery lead to cost savings in 99.1% of cases (-€8,408), and generated an additional 4.1 quality-adjusted life years (QALYs) per patient compared to medical treatment. Bariatric surgery was cost-effective with an incremental cost-effectiveness ratio (ICER) of €26,985/QALY after 2 years (willingness to pay threshold of €35,526/QALYs). In the diabetic cohort, bariatric surgery was cost-effective in all 4 categories: moderately (BMI 30 to 34), severely (BMI 35 to 39), morbidly (BMI 40 to 50) and super obese (BMI >50). In the non-diabetic cohort, bariatric surgery was cost-effective in all categories except for moderately obese patients (BMI 30 to 34)

A cost evaluation study in Spain assessed the cost-utility for severely obese patients undergoing gastric bypass (aged 18-55; mean BMI 50.7) compared to conventional treatment using a discrete-event simulation model with various time horizons.[16] Costs were direct medical costs of bariatric surgery and medical treatment and reported in 2012 €.

At five years, gastric bypass result in an additional spending of €3,350, and generated a loss of 0.13 QALYs per patient compared to medical treatment which may be due to high cost of surgery and the surgery-related deaths. At 10 years, gastric bypass result in an additional spending of €1,803, and generated an additional 0.45 QALYs per patient. At 15 years, gastric bypass result in an additional spending of €89.21, and generated an additional 1.12 QALYs per patient. At 20 years, gastric bypass result in a saving of €1,764, and generated an additional 1.82 QALYs per patient. Over a life time, compared to medical treatment, gastric bypass result in a saving of €13,994, and generated an additional 5.63 QALYs per patient.

Limitations

The evidence on the comparative long-term clinical effectiveness of bariatric surgery to conventional treatment is limited to one RCT with a relatively short 5 year follow-up period. The economic evaluations considered bariatric surgery as a whole, so it is unclear whether there are differences between different surgical approaches. The generalizability of the results of the economic studies to a Canadian context may be limited since context and cost data were based on foreign sources.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

At five years follow up, bariatric surgeries lead to a statistically significant reduction in weight, waist circumference and body mass index as compared to medical treatment in patients with morbid obesity. Evidence from cost evaluation studies showed that bariatric surgery is more cost-effective than conventional treatment in patients with morbid obesity over a life time horizon. Despite higher inpatient costs at 15 years with surgery, there was no difference in total health care costs in the subgroup of patients with diabetes, with savings mainly driven in reduced costs of diabetes drugs. Economic results should be interpreted with caution since context and cost data used foreign sources.

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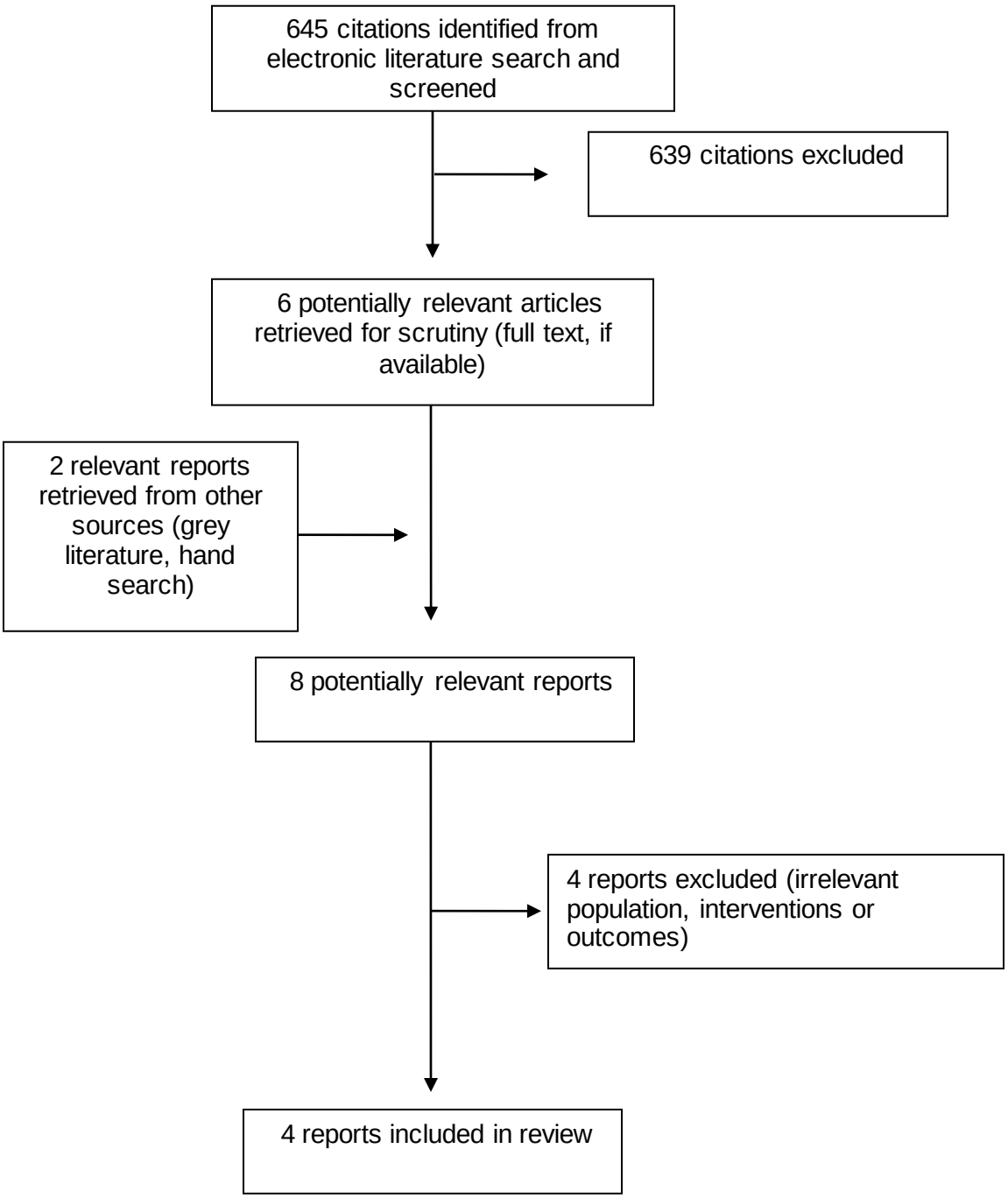
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Studies

Table A1: Characteristics of Included studies

First Author, Year, Country,	Study Objectives	Interventions/Comparators	Patients	Main Study Outcomes
Clinical studies				
Mingrone,[13] 2015, Italy, Germany, UK	"*We aimed to assess 5 year outcomes from our randomised trial designed to compare surgery with conventional medical treatment for the treatment of type 2 diabetes in obese patients*" (p 964)	Roux-en-Y (19 patients) Biliopancreatic diversion (19 patients) Medical treatment (15 patients)	*"Patients aged 30–60 years with a body-mass index of 35 kg/m^2 or more and a history of type 2 diabetes lasting at least 5 years"* (p 964)	Diabetic remission (at 5 years) Changes in weight, waist circumference and BMI (at 5 years)
Cost studies				
Keating,[14] 2015, Sweden	*"We aimed to assess health-care costs over 15 years for patients with obesity treated conventionally or with bariatric surgery and who had either euglycaemia, prediabetes, or type 2 diabetes before intervention"* (p 855)	Bariatric surgery (GBP, VBG, GB) Medical treatment	Obese patients undergoing bariatric surgery (mean age 47, SD 6; mean BMI ≥ 42.7 in men, SD 4.2 and ≥ 41.2 in women, SD 4.7)	Cost savings (2013 US$) (costs of health care use retrieved from Swedish registers: drug costs, inpatient costs, outpatient costs)
Borisenko,[15] 2015, Sweden	*"The objective of the present study was to evaluate the cost-utility of bariatric surgery in a lifetime horizon from a Swedish health care payer perspective"* (p 1559)	Bariatric surgery (GBP, SG, GB) Medical treatment	Obese patients undergoing bariatric surgery (mean age 41; range 25 – 65; mean BMI 42.8; range 30 – 60)	Cost evaluation: using Markow modeling with life time horizon; direct medical costs (2012 €): costs of bariatric surgery; costs of medical treatment ICER QALY
Castilla,[16] 2014, Spain	*"To assess the cost–utility of gastric bypass versus usual care for patients with severe obesity in Spain"* (p 2061)	Bariatric surgery (GBP)	Obese patients undergoing gastric bypass (aged 18-55; mean BMI 50.7; range 36.6-76.3)	Cost evaluation: using a discrete-event simulation (DES) modeling with various time horizons; direct medical costs (2012 €): costs of bariatric surgery; costs of medical treatment ICER QALY

GB : gastric banding; GBP: gastric bypass; ICER : incremental cost-effectiveness ratio; QALY : quality-adjusted life years; SD : standard deviation; SG : sleeve gastrectomy; VBG : vertical-banded gastroplasty

Appendix 3: Summary of Critical Appraisal of Included Study

Table A2: Summary of Critical Appraisal of Included Study

First Author, Publication Year	Strengths	Limitations
Critical appraisal of included clinical trials (Downs and Black)11)		
Mingrone,[13] 2015	• hypothesis clearly described • patients randomized • method of selection from source population and representation described • main outcomes, interventions, patient characteristics, and main findings clearly described • estimates of random variability and actual probability values provided • losses to follow-up described study had sufficient power to detect a clinically important effect	• Participants not blinded
Critical appraisal of included cost study (Drummond[12])		
Keating,[14] 2015	• outcomes and costs assessed and compared appropriately (all the important and relevant outcomes and costs for each alternative identified; outcomes and costs measured accurately in appropriate units prior to evaluation; outcomes and costs valued credibly; outcomes and costs adjusted for different times at which they occurred) • the presentation and discussion of study results include all issues of concern to users	• there was no economic evaluation performed • there was no incremental analysis performed • there was no sensitivity analysis performed • the generalizability of the results to a Canadian context may be limited since costs data used Swedish sources
Borisenko,[15] 2015	• the economic evaluation is likely to be usable (a well-defined question posed in an answerable form; a comprehensive description of the competing alternatives given; evidence for the programme's effectiveness established) • outcomes and costs assessed and compared appropriately (all the important and relevant outcomes and costs for each alternative identified; outcomes and costs measured accurately in appropriate units prior to evaluation; outcomes and costs valued credibly; outcomes and costs adjusted for different times at which they occurred) • an incremental analysis of the outcomes and costs of alternatives performed • a sensitivity analysis performed • the presentation and discussion of study results include all issues of concern to users	• the generalizability of the results to a Canadian context may be limited since costs data used Swedish sources

Table A2: Summary of Critical Appraisal of Included Study		
First Author, Publication Year	**Strengths**	**Limitations**
Castilla,[16] 2014	• the economic evaluation is likely to be usable (a well-defined question posed in an answerable form; a comprehensive description of the competing alternatives given; evidence for the programme's effectiveness established) • outcomes and costs assessed and compared appropriately (all the important and relevant outcomes and costs for each alternative identified; outcomes and costs measured accurately in appropriate units prior to evaluation; outcomes and costs valued credibly; outcomes and costs adjusted for different times at which they occurred) • an incremental analysis of the outcomes and costs of alternatives performed • a sensitivity analysis performed • the presentation and discussion of study results include all issues of concern to users	• the generalizability of the results to a Canadian context may be limited since costs data used Spanish sources

Appendix 4: Main Study Findings and Authors' Conclusions

Table A3: Main Study Findings and Authors' Conclusions

First Author, Publication Year	Main Study Findings	Authors' Conclusions
Research question 1 (long-term clinical effectiveness of bariatric surgery for the treatment of obesity and morbid obesity)		
Mingrone,[13] 2015	At 5 years Weight (kg) (mean; SD) Medical treatment: 127.1 (20.5) Gastric bypass (Roux-en-Y): 90.3 (12.7) Biliopancreatic diversion: 92.8 (14.0) *P* < 0.0001 Waist circumference (cm) Medical treatment: 113.9 (14.2) Gastric bypass (Roux-en-Y): 101.5 (12.8) Biliopancreatic diversion: 102.4 (12.6) *P* < 0.0170 BMI (kg/m^2) Medical treatment: 42.1 (5.8) Gastric bypass (Roux-en-Y): 31.3 (2.5) Biliopancreatic diversion: 30.3 (4.0) *P* < 0.0001 Diabetes remission (number of participants, %) Medical treatment: 0 (0%) Gastric bypass (Roux-en-Y): 7 (37%) Biliopancreatic diversion: 12 (63%) *P* =0.0007 HbA_{1c} concentration ≤6.5% Medical treatment: 4 (27%) Gastric bypass (Roux-en-Y): 8 (42%) Biliopancreatic diversion: 13 (68%) *P* =0.0457	*"In summary, surgery is more effective than medical treatment for the long-term control of obese patients with type 2 diabetes"* (p 972)
Research question 2 (long-term cost effectiveness of bariatric surgery for the treatment of obesity and morbid obesity)		
Keating,[14] 2015	Costs over 15 years Drug costs did not differ between the surgery and conventional treatment group in patients with euglycaemia ($10 511 *vs* $10 680; adjusted mean difference -$225; *P*=0.812), but were lower in the surgery group in the prediabetes ($10 194 *vs* $13 186; –$3329; P=0.007) and diabetes group ($14 346 *vs* $19 511; –$5487 *P*<0.0001) Inpatient costs: higher in the surgery group for all 3 groups than in the conventional treatment. Euglycaemia group ($51 225 *vs* $25 313; $22 931; *P*<0.0001), prediabetes ($58 699 *vs* $32 861; $27 152; *P*<0.0001), and diabetes ($61 569 *vs* $47 569; $18 697; *P*<0.0001) Outpatient costs: no difference in all 3 groups Total health-care costs: higher in the surgery group in the	*"Total health-care costs were higher for patients with euglycaemia or prediabetes in the surgery group than in the conventional treatment group, but we detected no difference between the surgery and conventional treatment groups for patients with diabetes"* (p 855)

Table A3: Main Study Findings and Authors' Conclusions		
First Author, Publication Year	**Main Study Findings**	**Authors' Conclusions**
	euglycaemic ($71 059 *vs* $45 542; $22 390; *P*<0.0001) and prediabetes ($78 151 *vs* $54 864; $26 292; *P*<0.0001) groups than in the conventional treatment group; no difference between treatment groups in patients with diabetes ($88 572 *vs* $79 967; $9081; *P*=0.090).	
Borisenko,[15] 2015	Costs over a life time Compared to medical treatment, surgery lead to a saving of €8,408 (€26,258 vs €34,665), and generated an additional 4.1 QALYs per patient. Sensitivity analysis showed that bariatric surgery produced clinical benefits (additional QALYs) in all patients and was cost saving in 99.1% of cases In general, bariatric surgery was cost-effective: ICER: €26,985/QALY after 2 years (willingness to pay threshold of €35,526/QALYs) In the diabetic cohort, bariatric surgery was cost-effective in all 4 categories: moderately (BMI 30 – 34), severely (BMI 35 – 39), morbidly (BMI 40 – 50) and super obese (BMI >50) In the non-diabetic cohort, bariatric surgery was cost-effective in all categories except for moderately obese patients (BMI 30 – 34)	*"Bariatric surgery, over a lifetime horizon, may lead to significant cost savings to health care systems in addition to the known clinical benefits"* (p 1559)
Castilla,[16] 2014	Costs at 5 years Compared to medical treatment, gastric bypass result in an additional spending of €3,350, and generated a loss of 0.13 QALYs per patient (medical treatment is better). Costs at 10 years Compared to medical treatment, gastric bypass result in an additional spending of €1,803, and generated an additional 0.45 QALYs per patient. Costs at 15 years Compared to medical treatment, gastric bypass result in an additional spending of €89.21, and generated an additional 1.12 QALYs per patient. Costs at 20 years Compared to medical treatment, gastric bypass result in a saving of €1,764, and generated an additional 1.82 QALYs per patient. Costs over a life time Compared to medical treatment, gastric bypass result in a saving of €13,994, and generated an additional 5.63 QALYs per patient.	*"Gastric bypass is an intervention that dominates over the option of not intervening when a lifetime horizon is considered"* (p 2061)