TITLE: Bariatric Surgery for Obese Patients with Co-Morbidities: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines

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CONTEXT AND POLICY ISSUES

Obesity is generally defined as a body mass index (BMI) of 30 kg/m^2 or more, with morbid, or extreme, obesity being a BMI ≥40 kg/m^2.[1] Approximately 23% of Canadians are obese,[1,2] which puts them at higher risk for obesity-related comorbidities such as obstructive sleep apnea, hypertension, hyperlipidemia and type II diabetes mellitus In 2004, more than 20% of Canadians with obesity had comorbid hypertension and for both men and women, obese adults are approximately five times more likely to have type II diabetes than their normal weight counterparts.[3] Not only are these conditions costly to treat, but obesity can reduce life expectancy by between five and 20 years, and represents a major cause of preventable death.[4]

Bariatric surgery involves gastric restriction, intestinal diversion, or a combination of both.[1] Gastric restriction restricts the volume of food that can be consumed and increases the feeling of satiety, while intestinal diversion reduces calorie absorption. The procedures are now more commonly performed laparoscopically, but open procedures are still occasionally done; common techniques include: biliopancreatic diversion (BPD), adjustable gastric banding (AGB; laparoscopic/LAGB or open), Roux-en-Y gastric bypass (RYGB), and sleeve gastroscopy (SG; laparoscopic/LSG or open).
The goal is to achieve drastic weight reduction and thus bariatric surgery is considered a treatment option for patients with obesity, particularly, for patients with comorbid conditions such as diabetes, sleep apnea, hypertension, and hyperlipidemia.[2]

The objective of this report is to review the comparative clinical effectiveness, safety, and cost-effectiveness of bariatric surgery for obese and morbidly obese patients with type II diabetes, sleep apnea, hypertension, and hyperlipidemia, as well as to review the relevant evidence-based guidelines, in order to help prioritize patients for bariatric surgery, based on comorbid conditions.

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness and safety of bariatric surgery for obese and morbidly obese patients with co-morbidities?

2. What are the evidence-based guidelines regarding bariatric surgery for obese and morbidly obese patients with co-morbidities?

3. What is the comparative cost-effectiveness of bariatric surgery for obese and morbidly obese patients with co-morbidities?

KEY FINDINGS

Ten systematic reviews (six pertaining to type II diabetes, one to sleep apnea, and three to hypertension or hyperlipidemia), two guidelines, and eight cost-effectiveness analyses (seven pertaining to type II diabetes only, one to type II diabetes, sleep apnea, hypertension, and hyperlipidemia) were included in the review. There is more evidence suggesting that patients with type II diabetes experience a resolution of comorbid disease following bariatric surgery and that the surgery is cost-effective, however the included studies examining sleep apnea, hypertension, and hyperlipidemia also found surgery to be helpful in the resolution of the comorbid condition. Bariatric procedures were also found to be cost-effective for sleep apnea, hypertension, and hyperlipidemia. The included guidelines indicate that type II diabetes may be an independent selection criterion for bariatric surgery in obese patients. Limited long-term safety information was identified.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2013, Issue 6), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, economic studies, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2008 and July 3, 2013.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed for relevance. Full texts of any relevant titles or abstracts were retrieved, and assessed for inclusion. The final article selection was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria	
Population	Obese (BMI 35-39.9 kg/m^2) or morbidly obese (BMI ≥ 40 kg/m^2) patients with co-morbidities. Co-morbidities are limited to: type 2 diabetes, hypertension, hyperlipidemia, and sleep apnea, or combinations of these.
Intervention	Bariatric surgery (any type)
Comparator	Patients with specific co-morbidities listed above (i.e., compare the various subgroups of patients with co-morbidities against each other)
Outcomes	Q1: Clinical benefits or harms for specific subgroups of patients (weight change, all-cause mortality, control of comorbidities, medication burden, hospitalization, health-related quality of life, excision of redundant tissue after weight loss [body contouring], joint operations, reoperations, gastrointestinal disturbances, and surgical sequelae). Q2: Guidelines for bariatric surgery for patients with the specific co-morbidities, or prioritization of patients with certain co-morbidities. Q3: Cost-effectiveness of bariatric surgery for specific subgroups of patients.
Study Designs	HTA, SR, MA, cost-effectiveness studies, evidence-based guidelines Follow-up at least 1 year

BMI = body mass index; HTA = health technology assessment; kg/m = kilograms per meter; MA = meta-analyses; SR = systematic review

Exclusion Criteria

Studies were excluded from the review if they did not meet the aforementioned inclusion criteria. Due to the volume of literature identified, randomized controlled trials and non-randomized studies were excluded from the review. Systematic reviews or meta-analyses that sought to compare surgical types with each other and economic evaluations that were not cost-effectiveness analyses were also excluded. Furthermore, evidence-based guidelines that did not make recommendations regarding more than one of the subgroups of interest, as well as position statements, were also excluded.

Critical Appraisal of Individual Studies

Critical appraisal of the included studies was based on study design.

The methodological quality of the included systematic reviews and meta-analyses was evaluated using the "assessment of multiple systematic reviews" (AMSTAR).[5] AMSTAR is an 11-item checklist that has been developed to ensure reliability and construct validity of systematic reviews. The Appraisal of Guidelines for Research and Evaluation II (AGREE II)[6] was used to evaluate the quality of the included guidelines. The methodological quality of the included cost-effectiveness studies were assessed using the guidelines for appraisal of economic studies by Drummond et al.[7]

For the included studies a numeric score was not calculated. Instead, the strengths and limitations of the study were described.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 471 potential citations were identified by searching the bibliographic database, with 426 citations being excluded during the title and abstract screening based on their irrelevance to the questions of interest. The full text documents of the remaining 45 articles were retrieved. Four additional articles were identified by grey literature and hand search. Of the 49 articles examined in full text, 28 did not meet the inclusion criteria and were excluded; leaving 21 articles that reported 10 systematic reviews (SR),[8-17] 2 guidelines (3 reports),[18-20] and 8 cost-effectiveness analyses (CEA).[1,21-27]

A PRISMA diagram illustrating the study selection process is presented in Appendix 1.

Summary of Study Characteristics

What is the comparative clinical effectiveness and safety of bariatric surgery for obese and morbidly obese patients with co-morbidities?

Of the ten systematic reviews examining the effects of bariatric surgery on obese patients included in the review, six examined patients with diabetes,[8,9,11,12,16,17] one examined patients with sleep apnea,[10] and three examined patients with hypertension or hyperlipidemia.[13-15] Many of the studies included data from follow-up periods 12 or more months of length as well as less than 12 months. Any information on shorter follow-up times was excluded from this review.

<u>Patients with type II diabetes</u>
Most of the six the SRs examining diabetic patients were conducted in North America (one in Canada[16] and four in the United States;[8,9,11,17] one was conducted in China.[12]

Two studies examined specific bariatric surgical techniques in patients with diabetes.[11,16] The Canadian study[16] reviewed the effect of LSG on type II diabetes outcomes using data from non-randomized controlled studies (NRCSs) and case series involving 673 patients with type II diabetes and a BMI >30. The main outcomes examined were BMI, excess weight loss, and diabetes improvement or remission before and after surgery. An American study reviewed the effect of LAGB on type II diabetes outcomes in obese patients with diabetes using data from RCTs, NRCSs, case series (both published and unpublished, and retrospective data analyses involving 1,404 patients).[11] The main outcomes examined were excess weight loss, glycemic outcomes, and diabetes improvement or remission.

The remaining four studies examined the effect of various bariatric procedures on type II diabetes outcomes.[8,9,12,17] The AHRQ analysis[8] from the United States examined patients with diabetes or metabolic syndrome who had a BMI ≥30.0 to ≤34.9. With respect to the outcomes of interest, they examined data from RCTs, cohort studies, non-randomized controlled studies, and case series, with a focus on BMI, excess weight loss, and resolution or remission of diabetes. A second American SR examined the effect of bariatric surgery on weight change, BMI, and glycemic control using data from RCTs and observational studies involving approximately 810 patients.[9] The included Chinese study examined obese patients with type II diabetes and a BMI<35 and included data from 11 prospective and 3 retrospective studies involving 345 patients. The main outcomes were weight reduction and glycemic outcomes before or after surgery.[12] A third American study[17] sought to determine the effect of bariatric

surgery on weight loss and type II diabetes outcomes using data from RCTs, NRCs, comparative retrospective studies, case series (prospective and retrospective), and observational studies involving 135,236 patients. The main outcomes reported were excess weight loss and type II diabetes resolution or remission.

Patients with Sleep Apnea

The included SR examining patients with sleep apnea was conducted in Canada.[10] This study reviewed the efficacy of various bariatric surgical procedures in relieving sleep apnea using data from RCTs, non-randomized controlled studies, and case series involving 13,900 obese patients. The focus was on the incidence of sleep apnea, weight loss, and BMI before and after the surgical procedure.

Patients with Hypertension or Hyperlipidemia

Of the three systematic reviews examining patients with hypertension and/or hyperlipidemia, one was conducted in Canada[13] and two in the USA.[14,15] The Canadian study[13] reviewed the effect of laparoscopic sleeve gastroscopy (LSG) on hypertension in RCTs, case control studies, cohort studies, and case series involving 3,997 patients. The focus was on BMI reduction, and the improvement or resolution of hypertension before and after surgery. Both American studies examined the effect of any bariatric procedure on cardiovascular (CV) risk factors in obese patients.[14,15] One study included RCTs, case control studies, and cohort studies examining 19,543 patients with CV risk factors[14] and the other RCTs, non-randomized controlled studies, controlled studies, case control studies, and case series examining 16,867 patients.[15] Both American studies focused on weight loss, the improvement or resolution of hypertension or hyperlipidemia, as well as other CV risk factors such as fasting blood glucose.

Further detail for all subgroups is tabulated in Appendix 2, Table 2.

What are the evidence-based guidelines regarding bariatric surgery for obese and morbidly obese patients with co-morbidities?

Three citations reporting two evidence-based guidelines that made recommendations regarding 2 or more subgroups were identified. One of the guidelines was German[18,19] and the other was from the United States.[20] The German guideline updated a previous guideline and used the Association of Scientific Medical Societies in Germany methods for developing the guideline, which involved a systematic review, evidence grading, recommendation development, and consensus conferences.

The American Guideline sought to develop appropriateness criteria for bariatric surgery with respect to age, BMI, and severity of obesity-related comorbidities.[20] The process involved systematic literature reviews, evidence grading, and two rounds of expert panel discussions.

Further detail for all subgroups is tabulated in Appendix 2, Table 3.

What is the comparative cost-effectiveness of bariatric surgery for obese and morbidly obese patients with co-morbidities?

All of the included CEAs considered the cost-effectiveness of surgically induced weight loss on patients with type II diabetes,[1,21-27] and one also considered patients with sleep apnea, with hypertension, and with hyperlipidemia.[1] Three considered the health system in the United Kingdom,[21,22,27] two in the United States,[23,25] one in Australia,[26] one in Canada,[1] and one

considered Austria, Italy, and Spain.[24] The time horizons ranged from one[1] or two years[22,27] to the lifetime[1,23,26] and the majority considered a healthcare payer[21,22,27] or health system perspective.[1,26]

Further detail, including the assumptions made in the models, is tabulated in Appendix 2, Table 4.

Summary of Critical Appraisal

What is the comparative clinical effectiveness and safety of bariatric surgery for obese and morbidly obese patients with co-morbidities?

Many of the included systematic reviews and meta-analyses shared similar strengths and limitations. Authors of all of the included studies performed comprehensive literature searches, and provided sufficient information on both inclusion criteria and the included trials.[8-17] 'A priori' design for the study was provided (often as a reference or internet appendix) in four of the studies,[8,9,17,27] In most studies, it was clear that duplicate study selection and data extraction took place.[8-10,12,13,16,27] Duplicate study selection and data extraction was assumed to have occurred in three studies, [14,15,17] due to the fact that authors mentioned following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

One of the main limitations of many of the included studies was the lack of assessment of the scientific quality of the included studies. Seven of the included systematic reviews did not report or include documentation of assessment of scientific quality of the included studies.[10-16] As the majority of the reviews included studies that were not randomized, and did not have a separate control group (patients acted as their own controls – before and after surgery),[8-12,14-17] this is especially problematic. Without assessing the potential biases in the included studies, the summary estimates provided by the studies may over-estimate the effect of bariatric surgery. Furthermore, when the risk of bias or quality of the included studies is not assessed, it is therefore unlikely that the scientific quality was considered when making conclusions. Many authors, however, were explicit in stating that one of the limitations of their review was the lack of high quality randomized studies.[9,11,16,28]

Although the Agency for Healthcare Research and Quality (AHRQ) report[8] had good methodology and followed most of the guidelines for conducting a good systematic review outlined in PRISMA, the layout of the report was problematic and difficult to follow and some of the reporting was unclear – especially with respect to which studies certain data was referring to. This made interpreting the results difficult.

Additionally, Li et al. performed a meta-analysis using many different study types without reporting sensitivity analyses based on study design.[12] Although a random effects model was used when the chi-square test showed heterogeneity, there was little discussion of whether or not the results were prone to bias or were accurate due to the heterogeneity.

Further detail regarding the strengths and limitations is tabulated in Appendix 3, Table 5.

What are the evidence-based guidelines regarding bariatric surgery for obese and morbidly obese patients with co-morbidities?

The main strengths of the included guideline from Germany,[18,19] by Runkel et al., are that it was based on a systematic review of the literature, there was a clear scope and purpose, good stakeholder involvement (though it was unclear if patients were included), and the clarity of the presentation. The major limitations include that the full evidence-rating schema was not presented, it was unclear whether the guideline was reviewed by an external expert panel, and information regarding potential barriers to application, resource implications, or tools for implementing the guideline was missing.

The main strengths of the included guideline from the United States,[20] by Yermilov et al., are the clear scope and purpose and good stakeholder involvement (though it was unclear if patients were included). Although a systematic review of the literature was performed, the details were not presented in the publication and the criteria for selecting the evidence were not clearly described. This was a major limitation. Furthermore, not all of the recommendations were unambiguous, and the applicability of the guideline was not presented.

Further detail is tabulated in Appendix 3, Table 6.

What is the comparative cost-effectiveness of bariatric surgery for obese and morbidly obese patients with co-morbidities?

The included cost-effectiveness studies generally had more strengths than limitations. The research questions, type of analysis, discount rates, and resource uses and costs were generally well reported. The majority included a time horizon of 10 years or longer,[1,21-23,25-27] which is important when determining the cost-effectiveness of bariatric surgery for chronic diseases such as type II diabetes, hypertension, and hyperlipidemia. However, many used short-term clinical data to make projections over a long time-horizon[1,21,22,25,26] and it is therefore difficult to know how accurate those projections are.

Two studies[21,25] used data from the Core Diabetes Model to project clinical outcomes that were derived form a diabetic, not necessarily obese, population. This may limit the applicability of these reports.

From a Canadian perspective, the majority of the included CEAs did not use Canadian data, nor was their analysis from the Canadian healthcare perspective.[21-27] The CEA from Canada provided sufficient detail with respect to the rationale of inputs, source of the estimates, methods to value health states, as well as the details of the model.[1] Its main limitations were that the details of statistical tests were not clearly reported and that because data from subjects not included in the clinical trials was used as inputs into the model, there may be different success and failure rates and therefore, the results of this economic evaluation may not apply to other patient populations.

Further detail is tabulated in Appendix 3, Table 7.

Summary of Findings

What is the comparative clinical effectiveness and safety of bariatric surgery for obese and morbidly obese patients with co-morbidities?

Patients with type II diabetes

All of the included studies that focused primarily on patients with obesity and type II diabetes found bariatric surgery, regardless of the comparator, to be beneficial on both BMI and type II diabetes outcomes.[8,9,11,12,16,17]

For studies reporting 1 year outcomes:[8,9,11]

- BMI reductions following bariatric surgery ranged from 5[8] to 10.5kg/m^2.[9] BMI change following medical management, in the study one reporting a summary mean was 2.4,[9] which was significantly lower (P<0.001) than that of surgical management.
- Patients undergoing bariatric surgery lost significantly more weight (P<0.001) than those in the medical management group in the two studies reporting this outcome[8,9] and in the study reporting excess weight loss (EWL), the mean percentage EWL following BS was 34.8%.[11]
- The percentage of patients achieving type II diabetes resolution ranged from 50%[8] to 83.5%,[8] depending on the bariatric procedure.
- Percentage of patients discontinuing type II diabetes medications ranged from 36.4%[8] to 87.2%,[8] depending on the bariatric procedure
- In the study reporting the average number of type II diabetes medications being taken,[9] patients in the surgical groups were taking significantly fewer medications (P<0.001)following surgery (0.3 medications for patients who underwent gastric bypass and 0.6 medications for patients who underwent gastric sleeve procedures), than the medical management patients (3.0 medications)
- HbA1C level as a total of total hemoglobin decreased 2.6 to 3.7 percentage points in one SR[8] and in another SR, the percentage of BS patients with HbA1C <6.0 was significantly lower than that of those who had medical management.[9]

For studies reporting outcomes between 12 and 24 months:[9,11,16,17]

- BMI reductions following bariatric surgical procedures ranged from 4.0[9] to 11.5[16]
- Average EWL ranged from 47%[11,16] to 67.1%[17]
- The percentage of patients achieving type II diabetes remission or resolution ranged from 51%[11] to 83.5%.[9] In studies where a composite outcome of type II diabetes remission or improvement was reported, the percentage of patients achieving remission or improvement of type II diabetes ranged from 56.4%[9] to 97.1%[16]
- Mean reduction in the percentage of patients receiving type II diabetes medication ranged from 36.4%[9] to 87.2%.[8,9]
- Mean reduction in HbA1C levels ranged from 1.7[16] to 3.1[9]

For studies reporting outcomes ≥24 months:[8,9,11,12,17]

- BMI reductions following bariatric surgical procedures ranged from 4 to 8[8] depending on the procedure, and in the study that reported it,[9] patients undergoing bariatric surgery lost significantly more weight than medical management (P<0.001).
- In one study, patients undergoing a bariatric procedure lost a mean of 19.6 kg more than those managed medically (P<0.001),[9] and average EWL ranged from 44.8%[11] to 58%[17]

- The percentage of patients achieving type II diabetes remission following bariatric surgery ranged from 37.6%[11] to 80%.[12] In the study where a composite outcome of type II diabetes remission or improvement was reported, 97.1% of surgical patients achieved the outcome.[16]
- Mean reduction in HbA1C level was 2.59% (95% Confidence Interval [CI] 2.12 to 3.07%, P < 0.00001)[12] in one study. The percentage of patients with HbA1C <6.2 was significantly higher (P<0.001) in the surgical patients (80%) than the medical management patients (20%) in the study reporting it[9] and in one study, HbA1C level as a percentage of total hemoglobin decreased 1.8 to 3.1 percentage points, depending on the surgical procedure.[8]

One study reported a single outcome for a follow-up period ≥5 years. The AHRQ report[8] identified one study that examined 29 LAGB patients who maintained an average BMI reduction of 5.7.

Limited safety data was reported in the included systematic reviews – most authors found data to be scarce, heterogeneous,[17] or not reported for the patients with type II diabetes.[11,16] One study found no evidence regarding all-cause mortality, cardiovascular mortality and morbidity, peripheral arterial disease[8] and one study found few severe adverse events and reported 3.2% of patients with early complications and no late (after 30 days) complications.[12] One death (due to sepsis) reported at 20 months in a patient who underwent LAGB was reported in the AHRQ analysis.[8] Authors of one study reported the estimated short term mortality of bariatric surgery to be 0.28%[17] and the authors of one study concluded that the long-term safety was unknown.[9]

Further detail regarding the specific comparisons and other outcomes is tabulated in Appendix 4, Table 8.

Overall, the authors of the included systematic reviews concluded that for patients with type II diabetes and a BMI:

- between 30 and 35, bariatric surgery was an effective treatment[8,9] with respect to glucose and weight reduction;
- <35, bariatric surgery was safe and effective and that the long-term metabolic outcomes could be sustained[12]
- ≥35, bariatric surgery was likely an effective treatment with respect to type II diabetes outcomes,[11] may lead to type II diabetes remission[16,17] and may play an important therapeutic role for type II diabetes.[16]

The majority of authors also noted that there was insufficient evidence regarding long-term outcomes.[8,9,11]

Patients with Sleep Apnea

The systematic review examining the effect of bariatric surgery on patients with sleep apnea examined most bariatric procedures.[10] Analyses were conducted on RYGB, LAGB, LSG, BPD, and "mixed," which included various bariatric techniques. Mean follow-up time ranged from 19 months in BPD, to 34.4 months in LAGB and baseline BMI ranged from 39.4(±4.2) to 51.6(±8.3). EWL after the surgical procedures ranged from 46.1% with LSG to 75.2% with RYGB. Sleep apnea outcomes were reported as a resolution, improvement or a composite resolution or improvement. Resolution of sleep apnea ranged from 63% (mixed) to 82.3% (LSG)

and the range of the composite resolution or improvement ranged from 77% (LAGB) to 99% (LSG). Adverse events were not reported.

The authors concluded that bariatric surgery of any kind was effective for treating sleep apnea in obese patients. Further detail is provided in Appendix 4, Table 8.

Patients with hypertension or hyperlipidemia

The three systematic reviews[13-15] examining the effect of bariatric surgical procedures on patients with obesity and hypertension all used before and after surgery comparisons. The shortest follow-up time was 16.9 months and in that study, the mean EWL was 63.3%, decrease in BMI was 13.1, and hypertension was resolved or improved in 75% of patients.[13] Younger patients had greater resolution of hypertension, as did those who lost more weight. In the study with a mean follow-up time of 34 months,[15] the mean EWL was 52% (ranging from 42% to 69% depending on the procedure), remission or resolution of hypertension occurred in 68% of patients, and remission or resolution of hyperlipidemia occurred in 71% of patients. The longest follow-up time was a mean of 57.8 months[14] and in that study, the average EWL was 54.2%, resolution or improvement of hypertension occurred in 52.5% of patients, resolution or improvement of hyperlipidemia occurred in 65.2% of patients. Two of the studies also reported remission or improvement of type II diabetes in 75%[15] and 73.2%[14] of patients.

One SR reported adverse events: cardiovascular mortality occurred in 2.1% of bariatric surgery patients and 2.6% of control patients, however, this data was based on a single included study.[15]

Overall, authors concluded that bariatric surgery was effective in treating cardiovascular risk factors in patients with BMI >30[13,14] and >35.[15] Further detail is provided in Appendix 4, Table 8.

What are the evidence-based guidelines regarding bariatric surgery for obese and morbidly obese patients with co-morbidities?

The included German guideline, which sought to develop appropriate indications for patients with obesity, stated that type II diabetes may be an indication criterion for bariatric surgery for patients with BMI 30 to 35, and that those patients should be entered into trials (considered Grade C or “may do”).[18,19] It recommended that for patients with a BMI of 35 to 40 and with one or more comorbidities (including type II diabetes, cardiovascular risk factors, and sleep apnea), patients for whom other treatments have failed or are considered futile are candidates for bariatric surgery (considered Grade A or “must do”). They suggested that for patients with major comorbidities (especially with BMI>50), stepwise surgery may be needed (e.g. start with sleeve gastrectomy, continue to gastric bypass).

The included American guideline,[20] which sought to develop appropriateness criteria stratified by age, BMI, and comorbidity severity made the recommendations that bariatric surgery was appropriate for:

- patients with BMI ≥40
    - who are 19 to 55 years of age and suffer from type II diabetes, sleep apnea, hypertension, or hyperlipidemia of any severity
    - who are 65 years of age or older with type II diabetes and HbA1c >9, regardless of therapy, or 7–9 on maximal medical therapy; severe to moderate sleep apnea, hypertension (regardless of treatment), or dyslipidemia (regardless of treatment)

- patients with BMI 34 to 39
    - who are 19 to 64 years and suffer from type II diabetes, sleep apnea, hypertension, or hyperlipidemia of any severity
    - who are 65 years of age or older with all type II diabetes severity levels except HbA1c 7 to 9 who are not on maximal therapy, moderate to severe sleep apnea, or severe (despite maximal treatment) hypertension

- patients with BMI 32 to 34
    - who are 19 to 64 years with type II diabetes in the severe category.

Although the recommendations were not graded, sufficient agreement among the guideline development panelists to make a recommendation was present in all recommendations for patients with BMI≥30.[20] The only exception was for patients with BMI 30 to 31 aged 19 to 55 years with severe type II diabetes, sleep apnea, hypertension, or hyperlipidemia. The panel was undecided and could not determine if bariatric surgery was appropriate for those patients.

For further detail regarding the recommendations, see Appendix 4, Table 9

What is the comparative cost-effectiveness of bariatric surgery for obese and morbidly obese patients with co-morbidities?

Patients with type II diabetes
All of the included cost-effectiveness studies examined the cost-effectiveness of bariatric surgery in patients with type II diabetes.[1,21-27] The surgical management of patients with type II diabetes and obesity was found to be cost-effective[21-25,27] or cost-saving[1,24,26] in at least one scenario in all of the included studies. Longer time horizons (10 or more years) yielded better cost outcomes than shorter time horizons.

From the Canadian perspective, RYGB was dominant over medical management over the lifetime horizon, CAN$4,151/QALY over 20 years, and CAN$12,701/QALY over 10 years.[1]

Further detail is provided in Appendix 4, Table 10.

Patients with Sleep Apnea, Hypertension, or Hyperlipidemia
One of the included cost-effectiveness studies addressed the cost-effectiveness of bariatric surgery over a lifetime horizon in patients with sleep apnea, hypertension, or hyperlipidemia in a sensitivity analysis.[1] The incremental cost-effectiveness ratios were as follows:

- CAN$5,246/QALY for patients with sleep apnea
- CAN$8,659/QALY for patients with hypertension
- CAN$7,811/QALY for patients with hyperlipidemia.

Limitations

The included systematic reviews examining the effects of bariatric surgery on obese patients drew data from various study types, many of which are considered to be of low methodological rigour. Case series and cohort studies were included in many of the systematic reviews and much of the patient data for the included reviews, and thus this review, came from studies for which the patients acted as their own controls (before/after studies). Another limitation of this study involves the definition of the subgroups and outcomes of interest. Variations in the

definitions of remission of diabetes were not always consistent, nor were the definitions of "improvement" in hypertension and hyperlipidemia. Although all studies focused on patients with a BMI of at least 30, the average baseline BMI was much higher in many studies, thus it is possible that not all results are generalizable to those with BMI between 30 and 35.

Most of the studies included a higher percentage of women than men. Since similar percentages of the adult male and adult female populations are obese, it is possible, if bariatric surgery has a differential effect dependent in sex, that men are underrepresented in the studies.

Limited safety information was available in the included systematic reviews and meta-analyses; therefore, there is a limited ability to draw conclusions regarding the comparative safety of bariatric surgery for patients with type II diabetes, sleep apnea, hypertension, and hyperlipidemia.

The majority of the information identified was pertinent to patients with type II diabetes, thus it is more difficult to draw conclusions regarding the effectiveness of bariatric surgery on hypertension, hyperlipidemia, and sleep apnea. This is especially important with respect to the cost-effectiveness information. From a cost-effectiveness perspective, one study provided estimates for subgroups other than type II diabetes, and although it was a Canadian study, it was published in 2010 and the cost estimates may be out of date. Again from the cost-effectiveness perspective, the majority of the information identified was from a perspective other than the Canadian perspective and the results may not be generalizable.

As only two guidelines were identified that pertained to two or more subgroups of interest, the limited number of recommendations available is a limitation of this study. The included guidelines were published in 2009 and 2010 and therefore, it is possible that updated information would change the recommendation.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

This report aimed to assess the comparative clinical effectiveness, safety, and cost-effectiveness of bariatric surgery for obese and morbidly obese patients with co-morbidities, as well as to review the relevant evidence-based guidelines. Ten systematic reviews, two evidence-based guidelines, and eight cost-effectiveness analyses were included in the review.

With respect to clinical effectiveness, the majority of the included systematic reviews focused on the effect of bariatric surgery on patients with type II diabetes and comorbid obesity. Bariatric surgery was shown to be effective in leading to decreases in BMI and a high percentage of remission or improvement of type II diabetes in at follow-up periods of at least 2 years. Bariatric surgery was also found to be effective in leading to remission of sleep apnea in a high percentage of patients after two years (in the single included study). The remission or resolution of hypertension or hyperlipidemia occurred more than half of the time in follow-up periods longer than a year. In general, patients with type II diabetes had a greater percentage of EWL than those with sleep apnea, but there were higher rates of sleep apnea resolution than diabetes resolution.

Limited information was identified regarding the safety, especially the long-term safety, of bariatric surgery on patients with obesity and comorbid type II diabetes, hypertension, hyperlipidemia, or sleep apnea. Although the evidence appears to show that bariatric surgery is

relatively safe, the authors of majority of the studies were not able to make conclusions regarding the safety of bariatric procedures in patients with those specific comorbidities. The included guidelines recommended that comorbid type II diabetes may be an important selection criterion for bariatric surgery in obese patients. Although it did not meet the inclusion criteria for this review, this is consistent with recommendations from the Ontario Health Technology Advisory Committee[29] which recommend bariatric surgery on morbidly obese people (BMI ≥35) with diabetes over those without.

With respect to cost-effectiveness, most studies were pertinent to type II diabetes and showed bariatric surgery to be cost-effective, and in some cases, cost-saving for patients with obesity and comorbid type II diabetes. From a Canadian perspective, over the lifetime horizon, bariatric surgery (RYGB specifically), is cost-saving in patients with type II diabetes and in order of most to least, was cost-effective in patients with sleep apnea, hyperlipidemia, and hypertension.

Further study is required to determine long-term (>3 years) outcomes of bariatric surgery on patients with obesity and comorbid type II diabetes, sleep apnea, hypertension, and hyperlipidemia.

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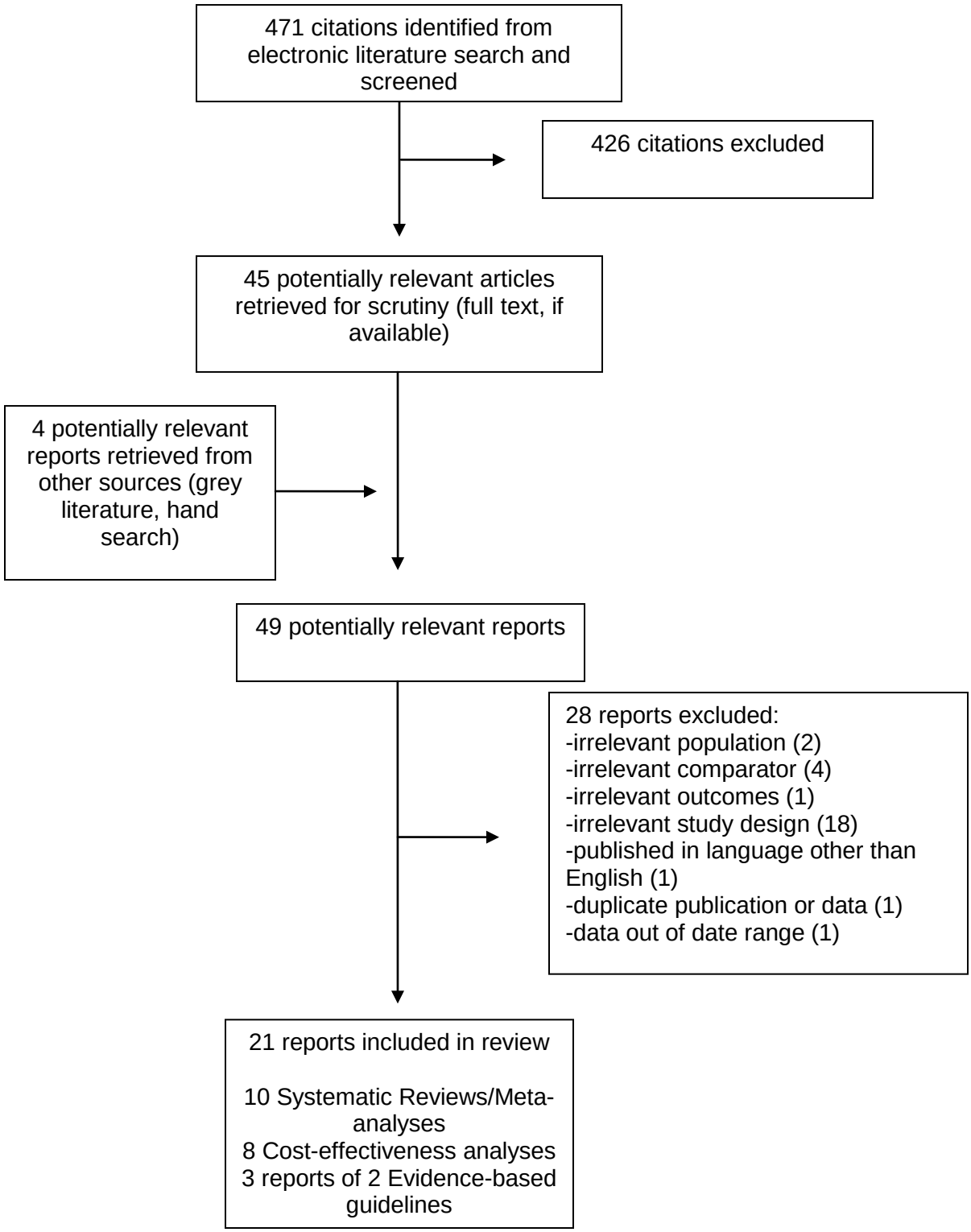
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Study Characteristics

Table 2: Characteristics of the Included Systematic Reviews and Meta-Analyses

Objectives, Scope	Type of primary studies included	Population Characteristics	Intervention	Comparator(s)	Clinical Outcomes; Length of follow-up
AHRQ, 2013, USA[8] – patients with metabolic conditions					
Determine efficacy and safety of bariatric surgery in patients with diabetes, metabolic syndrome	RCT • 3 studies CCS • 1 study NRCS, case series • 9 studies Cohort • 2 small	>491 adult patients with diabetes or with metabolic syndrome, BMI ≥30.0 to ≤34.9 Summary baseline BMI, age, gender distribution not reported. (baseline BMI in 2 of the included RCTs: 37.0 kg/m2	LAGB, RYGB, BPD, SG	Non-surgical treatments, before/after	EWL, FBG, BMI, DM2 resolution (defined as defined as HgA1c<6.5 percent and fasting blood glucose<100 mg/dL) 3[b] – >24 months
Maggard-Gibbons, 2013,[9] USA – patients with diabetes					
Assess association between bariatric surgery vs. medical management, and weight loss & glycemic control in patients with diabetes and BMI ≥30 to ≤35.	RCTs • 2 studies Observational studies: • ~8 studies (unclear reporting)	RCTs: 210 adult patients with DM2; BMI ≥30 to ≤35 Observational Studies: ~600 patients (unclear reporting	Surgical Interventions	Non-Surgical[a] Before/after	Weight change, BMI, Fasting Blood glucose, No. patients with HbA1c <6.0%, Avg. no. diabetes medication, diabetes remission 12 to 24 months
Sarkosh, 2013,[10] Canada – patients with sleep apnea					
Review the efficacy of bariatric surgery in relieving obstructive sleep apnea in obese adults.	RCTs • 3 studies NRCS • 11 studies Case series • 55 studies	13,900 Adults with obesity undergoing bariatric surgery RYGB = 5,430	Bariatric Surgery (RYGB, LAGB, LSG, BPD)	Before/after	Incidence of sleep apnea, mean BMI, EWL

Table 2: Characteristics of the Included Systematic Reviews and Meta-Analyses					
Objectives, Scope	**Type of primary studies included**	**Population Characteristics**	**Intervention**	**Comparator(s)**	**Clinical Outcomes; Length of follow-up**
	13,900 patients total; surgical procedures: • RYGB (36 studies) • LAGB (21 studies) • LSG (8 studies) • BPD (4 studies)	patients;45.4 ±8.5 yrs; 69% female; preop BMI = 51.6±8.3 LAGB = 4,095; 41.8± 6.9 years; 74% female; preop BMI = 46.1±5.2 LSG: 543 patients; 39.4±4.2; ; 64% female; preop BMI 47.7±4.9 BPD: 246 patients; 40.7±4.3 years; preop BMI = 50.5±4.9 MIX = 3,586 patients 42.2±4.4 years; 56% women; preop BMI 48.3±5.6			
Dixon, 2012,[11] USA – patients with diabetes					
Evaluate the effect of LAGB on diabetes outcomes in obese patients with DM2	RCTs • 1 study NRCS • 4 studies Case series • 23 studies (5 unpublished) Retrospective data analyses • 2	Adult LAGB patients with DM2 12 months: 696 pts. mean age 45.4 yrs; 72% female; preop BMI 45.2 15 to 24 months: 247 pts, mean age 39.4 yrs, 74.2% female, baseline BMI 44	LAGB	Before/after surgery	Weighted average DM2 remission rate (defined as a return to 'normal' HbA1C level), diabetes improvement, EWL, HbA1c improvement, FBG improvement 6 months[b] 12 months 15-24 months ≥24 months

Table 2: Characteristics of the Included Systematic Reviews and Meta-Analyses					
Objectives, Scope	**Type of primary studies included**	**Population Characteristics**	**Intervention**	**Comparator(s)**	**Clinical Outcomes; Length of follow-up**
		≥24 months: 461 pts; 43.9 years, 70.8% female; preop BMI 46.1			
Li, 2012, China[12] – patients with diabetes					
Assess the metabolic effects of bariatric surgery in patients with DM2 and BMI <35	All study designs 11 prospective 3 retrospective	367 (345 for 12 month or longer follow-up) patients with DM2 and BMI <35 Age range: 22 to 66 yrs (mean NR) baseline BMI 29.72, 52.2% female	RYGB, DJB, BPD, MGB, sleeve gastrectomy	Before/after surgery	Weight reduction, BMI, FPG, HbA1c, Insulin 6 months[b]-5 years
Sarkhosh, 2012, Canada,[13] – patients with hypertension					
Review the effect of LSG on hypertension	RCTs • 1 study CCS • 1 study Cohort • 11 studies Case series • 20 studies	Adults with hypertension 3,997 patients 42.23±4.4 yrs, 67% female, preop BMI 49.1±7.5	LSG	Before/after surgery	BMI, resolution of hypertension, improvement of hypertension 12-48 months
Vest, 2012, USA[14] – patients with cardiovascular risk factors					
To examine the impact of bariatric surgery on patients with CV risk factors	RCTs, CCS, Cohort	19,543 patients undergoing bariatric surgery, with CV risk factors 41.7 years, 76% women, baseline MBI 47.1	Any bariatric procedure (RYGB + GBP = 57%, GB: 27%)	Before/after surgery	EWL, resolution or improvement in: hypertension, hyperlipidemia and diabetes 12-176 months
Heneghan, 2011, USA[15] – patients with cardiovascular risk factors					
To evaluate the impact of bariatric surgery on morbidly obese	RCT • 2 studies NRCS • 3 studies	16,867 patients, 42 yrs, 78% women, preop BMI 49 Baseline	Any bariatric procedure (RYGB, BPD most common)	Before/after surgery	EWL, remission/resolution of comorbidities Change in FBG 3-55 months; average 34 months

Table 2: Characteristics of the Included Systematic Reviews and Meta-Analyses					
Objectives, Scope	**Type of primary studies included**	**Population Characteristics**	**Intervention**	**Comparator(s)**	**Clinical Outcomes; Length of follow-up**
patients with CV risk factors	CS • 5 studies CCS • 2 studies Case Series • 40 studies	comorbidities: Hypertension: 49% DM: 28% Dyslipidemia: 46%			
Gill, 2010, Canada[16] – patients with diabetes					
Review the effect of LSG on DM2	RCTs • 0 included NRCS • 6 studies Case Series • 21 studies	673 adult patients, DM2, BMI >30, undergoing LSG 46.6±3.8 years, 66% women, BMI 47.4	LSG as a single procedure or as part of a staged bariatric intervention	Before/after surgery	BMI, EWL, DM2 resolution (defined as discontinuation of hypoglycemic medications, and/or insulin, normal fasting glucose, normal HbA1C), DM2 improvements
Buchwald, 2009, USA[17] – patients with diabetes					
Determine the impact of bariatric surgery weight loss and diabetes outcomes	RCT • 29 studies NRCS • 40 CR • 60 RUCS • 187 Observational • 25 Case series • 2	135,236 patients 40.2 years, 79.6% female, BMI 47.9	Bariatric surgery (gastric banding, gastroplasty, gastric bypass, BPD/ duodenal switch	Before/after surgery	EWL, DM2 resolution (defined as the resolution of the clinical and laboratory manifestations of type 2 diabetes), DM2 improvements <2 yrs ≥2 yrs

BPD = biliopancreatic diversion; CCS = case-control studies; CR = comparative retrospective; CS = controlled studies; CV = cardiovascular; DJB = duodenal–jejunal exclusion surgery; EWL = excess weight loss; FBG = fasting blood glucose; HbA1c = hemoglobin A1c; LAGB = laparoscopic adjustable gastric banding; LSG = laparoscopic sleeve gastroscopy; MGB = mini-gastric bypass; RUCS = retrospective uncontrolled case series RYGB = Roux-en-Y gastric bypass; yrs = years
[a]Direct and indirect comparisons [b]Data from follow-up periods shorter than 1 year not included in this review; [c] only relevant subgroups reported in this review

Table 3: Characteristics of the included Evidence-based Guidelines				
Author, Year, Country of Origin	**Purpose**	**Comorbidities considered**	**Definition**	**Severity**
Runkel[18,19] 2010, Germany	To provide information on the appropriate indications and procedures for the treatment of morbid obesity (BMI 30-35) in Germany	DM2, cardiovascular risk factors, sleep apnea	NR	NR
Yermilov, 2009,[20] USA	To develop appropriateness criteria for bariatric surgery and to stratify according to BMI, age, and comorbidity severity.	DM2	Treatment with insulin, oral hypoglycemic medications, or fasting glucose >126 mg/dL	1. HbA1c >9, on maximal medical therapy 2. HbA1c >9, not on maximal medical therapy 3. HbA1c 7–9, on maximal medical therapy 4. HbA1c 7–9, not on maximal medical therapy 5. HbA1c <7, regardless of therapy
		Hypertension	Systolic Blood Pressure >140 or Diastolic Blood Pressure >90, or use of antihypertensive medication	1. Dyslipidemic on maximal medical therapy 2. Dyslipidemic not on maximal medical therapy 3. Nondyslipidemic on maximal medical therapy 4. Nondyslipidemic, not on maximal medical therapy
		Dyslipidemia	Triglycerides >250 mg/dl or cholesterol >220 mg/dl or HDL <35 mg/dl or LDL >200 or use of lipid lowering medication	1. Dyslipidemic on maximal medical therapy 2. Dyslipidemic not on maximal medical therapy 3. Nondyslipidemic on maximal medical therapy 4. Nondyslipidemic, not on maximal medical therapy
		Sleep Apnea	Formal Sleep tests with the results of: • Epworth Sleepiness Scale ≥6; • Polysomnography with Respiratory Disturbance Index ≥10 hyponeic and/or apneic episodes per hour of sleep	1. Severe (e.g., apnea–hypoapnea index >30 per hour) 2. Moderate (e.g., apnea–hypoapnea index 16–30 per hour) 3. Mild (e.g., apnea–hypoapnea index 5–15 per hour)

dL = deciliter; DM2 = type 2 diabetes mellitus; HDL = high-density lipoproteins; HbA1c = hemoglobin A1c; LDL = low-density lipoproteins

Table 4: Study Characteristics of the Included Cost-Effectiveness Analyses

First author, Year	Country, perspective	Type of Surgery, Comparator	Study Population	Time Horizon	Main Assumptions
Pollock, 2013[21]	UK, healthcare payer perspective	LAGB vs. SMM	Simulated UK cohort of 1,000 obese patients with DM2	40 years	• 46.5% male • Mean baseline age 46.9 years (SD 8.9 years) • Mean baseline BMI 37.1 kg/m2 Mean HbA1c was 7.7% • Mean duration of DM2 1 year (SD 4 mo) • Sensitivity analysis BMI 42.4±4.5 kg/m^2 • 3.5% discount rate, 0-6% in sensitivity analyses
Picot, 2012[22]	UK, healthcare payer perspective	LAGB vs. non-surgical management	Class I and II obesity with DM2	2 years, 5 years, 20 years	• Assumed baseline BMI 33.5 kg/m^2 • Assumed cost of LAGB £4,546, • All procedures done laparoscopically • Assumed health state costs for diabetes include components of diabetes care • Base case – patients assumed to revert to pre-surgical weight after 10 years • 3.5% discount rate
Hoerger, 2010[23]	USA, perspective NR	GBP vs. usual diabetes care Gastric banding vs. usual diabetes care	Obese patients with newly diagnosed DM2, obese patients with long-standing DM2	Diagnosis to death or 95 years old	• BMI ≥35 kg/m2 • assumes that diabetes progression rates are homogeneous • diabetes duration 10 years • patients who were not in diabetes remission would also receive tight glycemic control • 3% discount rate
Klarenbach, 2010[1]	Canada, Canadian publicly funded health system perspective	RYGB vs. standard care	Obese patients with DM2, hypertension, hyperlipidemia, sleep apnea (subgroups within the analysis)	1 year, 10 years, 20 years, lifetime	• BMI 35 kg/m^2 or more with comorbidity • patient screened by specialists, trained psychologists to exclude patients unsuitable for surgery • 5% discount rate (0-3% in sensitivity

Table 4: Study Characteristics of the Included Cost-Effectiveness Analyses

First author, Year	Country, perspective	Type of Surgery, Comparator	Study Population	Time Horizon	Main Assumptions
					analysis) • Annual risk of mortality constant in first 10 yrs • Assumed no BMI change in non-surgical patients • Costs of treating comorbidities mutually independent • beyond 10 years, no change in prevalence of obesity-related comorbid conditions • for comorbid ICUR calculations, assumed 100% of population had the comorbidity
Anselmino, 2009[24]	Austria, Italy, Spain, payer perspective	AGB or GBP vs. conventional therapy	Obese patients with DM2	5 years	• 3.5% discount rate • BMI≥35 • Assumed AGB and GBP were 20% less effective (in terms of BMI reductions and DM2 remission) than literature estimates • Assumed conventional therapy was low-cost watchful waiting (no BMI reduction, no DM2 remission) • Annual cost of DM2 treatment assumed to be base case cost
Ikramuddin, 2009[25]	USA, 3rd party payer perspective	RYGB vs. standard medical management	Obese patients with DM2	35 years	• mean 50.1 years, 77.9% female, duration of disease 8.7 yrs, mean BMI 48.4 • 3% discount rate, 0-6% in sensitivity analyses
Keating, 2009[26]	Australia, health care system perspective	Surgically induced weight-loss vs. conventional treatment	Obese patients with DM2	Lifetime	• 3% discount rate • surgical therapy intervention assumed to be lifetime program (monitor and maintain weight loss) • patients assumed to have mean DM2 duration of 3 years at the end of the trial

Table 4: Study Characteristics of the Included Cost-Effectiveness Analyses

First author, Year	Country, perspective	Type of Surgery, Comparator	Study Population	Time Horizon	Main Assumptions
					• cumulative probability of a complication: 17%/10yrs
Picot, 2009[27]	UK, healthcare payer perspective	AGB vs. no surgery	Obese patients with DM2	2 years, 5 years, 20 years	• "no surgery" assumed to be associated with no weight loss • assumed, as with the • post-discharge routine for surgical patients, that • non-surgical patients would have more frequent consultations with dietitians than with general medical support • assumed that all patients with previously resolved DM2 remained in the post-diabetic state up to 10 years would then relapse and return to the diabetic health state

AGB = adjustable gastric bypass; BIA = budget impact analysis; CEA = cost-effectiveness analysis; DM2 = type 2 diabetes; GBP = gastric bypass; LAGB = laparoscopic adjustable gastric banding; NR = not reported; RYGB = Roux-en-Y gastric bypass; SMM = standard medical management; UK = United Kingdom; USA = United States of America

APPENDIX 3: Critical appraisal

Table 5: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[5]

Strengths	Limitations
AHRQ[8]	
• 'a priori' design provided • duplicate study selection and data extraction • comprehensive literature search performed • status of publication used as an inclusion criterion • list of studies (included and excluded) provided • characteristics of the included studies provided • scientific quality of the included studies assessed and documented • scientific quality of the included studies used appropriately in formulating conclusions • methods used to combine the findings of studies appropriate • conflict of interest stated	• Low strength of evidence • Populations of the included studies may not have been comparable • likelihood of publication bias not assessed graphically • Clarity of presentation – difficult to navigate the report
Maggard-Gibbons[9]	
• 'a priori' design provided • list of included studies provided • duplicate study selection and data extraction • comprehensive literature search performed • scientific quality of the included studies assessed and documented (eTables, not in main publication) • status of publication used as an inclusion criterion • characteristics of the included studies provided • conflict of interest stated • scientific quality of the included studies used appropriately in formulating conclusions • methods used to combine the findings of studies appropriate	• list of excluded studies not provided • likelihood of publication bias assessed • limited number of studies included • data not able to be pooled
Sarkosh[10]	
• comprehensive literature search performed • status of publication used as an inclusion criterion • duplicate study selection and data extraction • characteristics of the included studies provided	• 'a priori' design not reported • list of excluded studies not provided • assessment of scientific quality of the included studies not reported; not clear if used appropriately in formulating conclusions • likelihood of publication bias not reported

Table 5: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[5]	
Strengths	**Limitations**
• conflict of interest stated • methods used to combine the findings of studies appropriate	
Dixon[11]	
• comprehensive literature search performed • status of publication used as an inclusion criterion • list of included studies provided • characteristics of the included studies provided • likelihood of publication bias not assessed, but unpublished studies included in review • methods used to combine the findings of studies appropriate (MA not performed – significant heterogeneity) • conflict of interest stated	• 'a priori' design not provided • duplicate study selection and data extraction • list of excluded studies not provided • assessment of scientific quality of the included studies not reported; not clear if used appropriately in formulating conclusions
Li[12]	
• duplicate study selection and data extraction • status of publication used as an inclusion criterion • comprehensive literature search performed • list of included studies provided • characteristics of the included studies provided • conflict of interest stated • methods used to combine the findings of studies appropriate (meta-analysis performed, heterogeneity assessed)	• 'a priori' design not provided • list of excluded studies not provided • assessment of scientific quality of the included studies not reported – unclear if performed – therefore also unclear if the scientific quality was used in formulating conclusions • likelihood of publication bias not assessed, or assessment not reported
Sarkhosh[13]	
• duplicate study selection and data extraction • comprehensive literature search performed • status of publication used as an inclusion criterion • characteristics of the included studies provided • methods used to combine the findings of studies likely appropriate	• 'a priori' design provided • list of excluded studies not provided • assessment of the scientific quality of the included studies not reported, therefore, unclear if it quality was used appropriately in formulating conclusions • likelihood of publication bias assessed • conflict of interest stated
Vest[14]	
• comprehensive literature search performed • status of publication used as an inclusion criterion • duplicate study selection and data extraction not reported but likely done (PRISMA used)	• 'a priori' design provided • list of excluded studies not provided • assessment of the scientific quality of the included studies not reported, therefore, unclear if scientific quality used appropriately in formulating conclusions

Table 5: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[5]	
Strengths	**Limitations**
• characteristics of the included studies provided • methods used to combine the findings of studies likely appropriate • list of included studies provided • likelihood of publication bias assessed • conflict of interest stated	
Heneghan[15]	
• comprehensive literature search performed • status of publication used as an inclusion criterion • characteristics of the included studies provided • 'a priori' design not provided (but review was done according to a protocol and using PRISMA) • duplicate study selection and data extraction not reported (but assumed) • methods used to combine the findings of studies appropriate • conflict of interest stated	• list of excluded studies not provided • assessment of the scientific quality of the included studies not reported; unclear if scientific quality used in formulating conclusions • likelihood of publication bias mentioned, but not assessed
Gill[16]	
• status of publication used as an inclusion criterion • comprehensive literature search performed • duplicate study selection and data extraction • assessment of the scientific quality of the included studies reported • scientific appropriately in formulating conclusions quality used • characteristics of the included studies provided • methods used to combine the findings of studies appropriate • conflict of interest stated	• 'a priori' design not provided (likely done) • list of excluded studies provided • likelihood of publication bias not assessed • assessment of the scientific quality of the included studies not documented
Buschwald[17]	
• 'a priori' design used • comprehensive literature search performed • status of publication used as an inclusion criterion • assessment of the scientific quality of the included studies reported, documented • characteristics of the included studies provided • conflict of interest stated	• duplicate study selection and data extraction unclear • methods used to combine the findings of studies likely appropriate • list of excluded studies provided • scientific quality used appropriately in formulating conclusions • likelihood of publication bias assessed

Table 6: Strengths and Limitations of the included Guidelines using AGREE II[6]

Strengths	Limitations
Runkel[18,19]	
SCOPE AND PURPOSE • The overall objectives of the guideline are specifically described – to provide recommendations regarding indications, procedures, techniques, and follow-up care for bariatric surgery. • The health question(s) covered by the guideline is (are) specifically described. • The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described – however, an a priori definition of obesity was not provided. STAKEHOLDER INVOLVEMENT • The guideline development group includes individuals from relevant professional groups – surgical working group, obesity society, nutritional medicine, psychosomatic medicine and psychotherapy, methodological advisor. • The target users of the guideline are clearly defined - bariatric surgeons, physicians, other health care professionals, patients, health care providers, and insurers. RIGOUR OF DEVELOPEMENT • Systematic methods were used to search for evidence – systematic literature search. • The criteria for selecting the evidence are clearly described. • The strengths and limitations of the body of evidence are clearly described – evidence graded according to a schema. • The methods for formulating the recommendations are relatively clearly described – the literature search was updated, 2 formal consensus conferences took place, recommendations made based on strong consensus, approved by a panel of experts. • The health benefits, side effects, and risks have been considered in formulating the recommendations. • There is an explicit link between the recommendations and the supporting evidence – graded, recommendations are based on evidence. CLARITY OF PRESENTATION • Key recommendations are easily identifiable	STAKEHOLDER INVOLVEMENT • Not clear if the views and preferences of the patients or public were sought. RIGOUR OF DEVELOPEMENT • Full evidence grading schema not presented clearly. • Unclear if the guideline has been externally reviewed by experts prior to its publication. An expert panel approved the guidelines, unclear if they were different than the guideline developers. • A procedure for updating the guideline has not been provided, however, the publication is an update of a previous guideline. APPLICABILITY • The guideline does not describe facilitators and barriers to its application. • The guideline does not provide advice and/or tools on how the recommendations can be put into practice. • The potential resource implications of applying the recommendations have not been considered. • The guideline does not present monitoring or auditing criteria. EDITORIAL INDEPENDENCE • Unclear if the views of the funding body have influenced the content of the guideline.

Table 6: Strengths and Limitations of the included Guidelines using AGREE II[6]	
Strengths	**Limitations**
• The recommendations are specific. • The different options for management of the condition or health issue are clearly presented. EDITORIAL INDEPENDENCE • Competing interests of guideline development group members have been recorded and addressed.	
Yermilov[20]	
SCOPE AND PURPOSE • The overall objective(s) of the guideline is (are) specifically described – to develop appropriateness criteria for bariatric surgery. • The population to whom the guideline is meant to apply is specifically described – patients who may benefit from or be harmed by bariatric surgery. • The health question(s) covered by the guideline is (are) specifically described. STAKEHOLDER INVOLVEMENT • Experts in bariatric surgery consulted – bariatric surgeons, internists, endocrinologists. • The target users of the guideline are clearly defined – clinicians who are advising patients on whether or not bariatric surgery is appropriate. RIGOUR OF DEVELOPMENT • Systematic methods were used to search for evidence. • The methods for formulating the recommendations are clearly described. • The strengths and limitations of the body of evidence are clearly described. • The health benefits, side effects, and risks have been considered in formulating the recommendations. CLARITY OF PRESENTATION • Key recommendations are easily identifiable. • The different options for management of the condition or health issue are clearly presented. EDITORIAL INDEPENDENCE • Competing interests of guideline development group members have been recorded and addressed.	STAKEHOLDER INVOLVEMENT • Unclear if the views and preferences of the target population (patients, public, etc.) were sought. RIGOUR OF DEVELOPEMENT • The criteria for selecting the evidence are not clearly described. • The link between the recommendations and the supporting evidence is not explicit. • It is unclear if the guideline has been externally reviewed by experts prior to its publication. • A procedure for updating the guideline is not provided. CLARITY OF PRESENTATION • The recommendations are ambiguous. APPLICABILITY • The guideline describes facilitators and barriers to its application. • The guideline does not provide advice and/or tools on how the recommendations can be put into practice. • The potential resource implications of applying the recommendations are not mentioned. • The guideline does not present monitoring and/or auditing criteria. EDITORIAL INDEPENDENCE • Unclear if the views of the funding body have influenced the content of the guideline.

Table 7: Strengths and Limitations of the Cost-effectiveness studies using Drummond[7]

Strengths	Limitations
Pollock, 2013[21]	
• research question and economic importance was clearly stated • clear description of comparators (LAGB vs SMM) • relevant alternatives were compared • rationale was provided for choice of comparators • type of economic evaluation used was stated (CEA) • time horizon of costs and benefits was stated (40 years) • discount rates were stated and justified (3.5% annually in base case, 0% to 6% in sensitivity analyses) • currency and price data were recorded (2010 pounds sterling) • primary outcome measure was clearly stated (remission of T2DM) • viewpoints of the analysis were stated and justified (public payer perspective) • source of effectiveness estimates stated (data from a single RCT) • methods to value health states and other benefits were stated • details of models used are provided (v8.0 Core Diabetes Model) • choice of model and key parameters were justified • details of method or synthesis provided • methods of estimation of costs and quantities were identified • quantities of resources were reported separately from their units costs • approach to sensitivity analysis was provided and choice of variables justified (model was insensitive to changes) • answer to the study question was given (LAGB highly cost-effective vs SMM; ICER = £3602 per QALY gained) • conclusions and limitations were clearly presented	• regression models in the Core Diabetes Model used to project clinical outcomes were derived form a diabetic, not necessarily obese, population • generalizability of results may be limited due to the origin of the data used to populate the model (efficacy data from a trial conducted in Australia with predominately white patients) • cost-effectiveness may not be generalizable for populations with different ethnic characteristics • short-term clinical data was used to make projections over a 40 year time horizon • use of UK cost data may mean results are not generalizable
Picot, 2012[22]	
• type of economic evaluation used was stated (systematic review and CEA) • rationale and clear description of comparators (non-surgical) • time horizon of costs and benefits was stated (up to 20 years) • viewpoints of the analysis were stated and	• currency and price data were not specifically stated but results were reported in British pounds • details of adjustments for inflation or currency conversion not provided (indicated health state costs were adjusted to 2009/2010 prices but methods/conversions not specified)

Table 7: Strengths and Limitations of the Cost-effectiveness studies using Drummond[7]	
Strengths	**Limitations**
justified (public payer perspective) • discount rates were stated and justified (3.5% annually) • source of effectiveness estimates stated (2 RCTs) • incremental analysis was reported (2, 5, and 20 years) • primary outcome measure was clearly stated (weight loss and AEs from SR) • choice of model and key parameters were justified; details of models used were provided • quantities of resources were reported separately from their units costs • methods to value health states and other benefits were stated (taken from published sources) • approach to sensitivity analysis was provided and choice of variables justified (one-way sensitivity analyses) • answer to the study question was given (bariatric surgery appears to be cost-effective for people with class I or II obesity and diabetes, not for class I obesity alone) • conclusions followed from the data reported and are accompanied by limitations	• details of statistical tests were not provided • limitations imposed by clinical effectiveness data used to populate the model (follow-up in RCTs limited to 2 years, withdrawals and patients lost to follow-up were greater in surgical group in both RCTs) • weight loss tends were extrapolated past 2 years by using data that might have been outdated • AEs and complications reported in RCTs were not incorporated into the model • the simple linear model relating change in BMI to gain in utility includes assumptions • use of UK cost data may mean results are not generalizable
Hoerger, 2010[23]	
• research question and economic importance were clearly stated • type of economic evaluation used was stated (CEA) • clear description and rationale for choice of comparators (GBP or gastric banding vs usual diabetes care) • time horizon of costs and benefits was stated (diagnosis to death or 95 years) • discount rates were stated and justified (3% annually) • details and choice of model and key parameters were justified (Centers for Disease Control and Prevention-RTI Diabetes Cost-Effectiveness Model) • primary outcome measure was clearly stated (diabetes remission) • currency and price data and details of adjustments for inflation or currency conversion were provided (converted to 2005 US dollars using Consumer Price Index) • approach to sensitivity analysis was provided and choice of variables justified (one-way analyses) • incremental analysis was reported (2 and 10 years)	• viewpoints of the analysis were not clearly stated or justified • methods to value health states and other benefits were not stated • details of statistical tests were not provided • did not assess the cost-effectiveness of bypass vs banding • use of US cost data may mean results are not generalizable • included only diabetes-related costs saved as a result of remission, not all obesity-related costs • long-term impact of surgery on diabetes outcomes were simulated by the model as there was little direct data • model assumes that diabetes progression rates are homogeneous

Table 7: Strengths and Limitations of the Cost-effectiveness studies using Drummond[7]	
Strengths	**Limitations**
• methods of estimation of costs and quantities were identified • quantities of resources were reported separately from their units costs • answer to the study question was given (bypass – ICER = new diagnosis $7,000 per QALY and established diagnosis $12,000 per QALY; banding – ICER = new diagnosis $11,000 per QALY and established diagnosis $13,000 per QALY)	
Klarenbach, 2010[1]	
• research question and economic importance were clearly stated • rationale was provided for choice of comparators (RYGB vs standard medical management) • type of economic evaluation used was stated (CEA) • viewpoints of the analysis were stated and justified (Canadian publicly funded health system) • time horizon of costs and benefits was stated (lifetime) • discount rates were stated and justified (5% annually, 0% and 3% in sensitivity analyses) • incremental analyses were reported (1 year, 10 years, and 20 years) • currency and price data were recorded (2009 Canadian dollars) and details of adjustments for inflation or currency conversion were provided (consumer price index) • source of effectiveness estimates stated (systematic review and observational studies) • methods to value health states and other benefits were stated • details of method or synthesis provided • approach to sensitivity analysis was provided and choice of variables justified • details of models used are provided • quantities of resources were reported separately from their units costs and methods of estimation of costs and quantities were identified • answer to the study question was given and conclusions followed from the data reported and are accompanied by limitations	• details of statistical tests were not clearly presented • because subjects not included in the clinical trials used for inputs to the model may have a different outcome and failure rate, the results of this economic evaluation may not apply to other patient populations • use of Canadian cost data may limit generalizability of the results to other jurisdictions • short-term trail data was used to model long-term clinical outcomes
Anselmino[24]	
• research question and economic importance were clearly stated • type of economic evaluation used was stated	• methods to value health states and other benefits were not stated • details of adjustments for inflation or currency

Table 7: Strengths and Limitations of the Cost-effectiveness studies using Drummond[7]	
Strengths	**Limitations**
(CEA and BIA) • time horizon of costs and benefits was stated (5 years) • discount rates were stated and justified (3.5% annually) • clear description and justification of choice of comparators • quantities of resources were reported separately from their units costs • choice of model and key parameters were justified and described • methods of estimation of costs and quantities were identified • answer to the study question was given (compared with conventional treatment at 5 years, AGB and GBP represent satisfactory value for money from the payer perspective).	conversion were not provided • details of statistical tests were not provided • incremental analysis was not reported • worst-case scenario over 5 years was conducted in lieu of sensitivity analyses • use of European cost data may mean results are not generalizable to other jurisdictions
Ikramuddin, 2009[25]	
• research question and economic importance were clearly stated • rationale was provided for choice of comparators (RYGB vs standard medical management) • time horizon of costs and benefits was stated (35 years) • discount rates were stated and justified (3.5% annually in base case, 0% and 6% in sensitivity analyses) • type of economic evaluation used was stated (CEA) • viewpoints of the analysis were stated and justified (third party payer perspective) • source of effectiveness estimates stated (one non-randomized study) • choice of model and key parameters provided (CORE Diabetes Model) • approach to sensitivity analysis was provided and choice of variables justified • incremental analysis was reported (5, 10, and 35 years) • quantities of resources were reported separately from their units costs • methods of estimation of costs and quantities were identified • RYGB was cost-effective when compared to standard medical management under base-case conditions	• regression models in the Core Diabetes Model used to project clinical outcomes were derived form a diabetic, not necessarily obese, population • details of adjustments for inflation or currency conversion were not provided • details of statistical tests were not provided • there is a lack of robust clinical data directly comparing bariatric surgery with standard management of diabetes • analysis excluded costs of other potentially required procedures resulting from significant weight loss • only patients with complete data on all parameters needed for the model were included. This may have biased the results in favor of surgery • positive effects of weight loss on other comorbid conditions not directly assessed by the model were not included in the analysis • short-term clinical data was used to model long-term outcomes
Keating, 2009[26]	
• research question was clearly stated and rationale was provided for choice of comparators	• the outcomes used to populate the model were specific to diabetes, and were not necessarily focussed on other outcomes related to weight

Table 7: Strengths and Limitations of the Cost-effectiveness studies using Drummond[7]	
Strengths	**Limitations**
• type of economic evaluation used was stated (CEA) • viewpoints of the analysis were stated and justified (health care system perspective) • time horizon of costs and benefits was stated (death or 99 years) • discount rates were stated and justified (3% annually) • currency and price data were recorded (2006 Australian dollars) • details of adjustments for inflation or currency conversion were provided • choice of model and key parameters were justified and detailed • details of method or synthesis provided • primary outcome measure was clearly stated (diabetes remission) • source of effectiveness estimates stated (data from one RCT) • methods of estimation of costs and quantities were identified • quantities and costs of resources were clearly reported • approach to sensitivity analysis was provided and choice of variables justified • answer to the study question was given • conclusions followed from the data reported and are accompanied by limitations	loss or additional benefits related to glycemic control in patients who did not enter diabetes remission • details of statistical tests were not provided • incremental analyses were not reported • long-term, lifetime modelling of outcomes was based on short-term trial results • generalizability of the CEA results to other populations may be limited. Treatment and intervention costs vary among patient populations and regions
Picot, 2009[27]	
• research question and economic importance clearly stated • rationale was provided for choice of comparators • viewpoints of the analysis were stated and justified (UK health care payer perspective) • type of economic evaluation used was stated (CEA) • time horizon of costs and benefits was stated (20 years) • discount rates were stated and justified (3.5% annually; 0% and 6% for costs, 0% and 1.5% for outcomes in sensitivity analyses) • incremental analyses were reported (2 years, 5 years) • details of adjustments for inflation or currency conversion were provided • details of models used, method or synthesis provided • source of effectiveness estimates stated • choice of model and key parameters were justified	• details of statistical tests were not clearly presented • long-term modelling of outcomes was based on short-term trial results • the majority of patients recruited in the clinical trials used for model input did not have major comorbidities associated with obesity • there was a wide variation in the ages of patients used to input the model • studies used in the model were conducted in various countries which may limit generalizability of cost estimates and clinical outcomes • weight loss was the major outcome in the model, however, not all clinical studies used for input were powered on a measure of weight loss • positive effects of weight loss on other comorbid conditions and costs of complications were not directly assessed by the model • the authors indicated there was uncertainty around resource use and costs associated with

Table 7: Strengths and Limitations of the Cost-effectiveness studies using Drummond[7]	
Strengths	**Limitations**
• methods to value health states and other benefits were stated • quantities of resources were reported separately from their units costs • methods of estimation of costs and quantities were identified • approach to sensitivity analysis was provided and choice of variables justified	surgical management

AE = adverse event; AGB = adjustable gastric bypass; BIA = budget impact analysis; BMI = body mass index; BIA = budget impact analysis; CEA = cost-effectiveness analysis; GBP = gastric bypass; ICER = incremental cost-effectiveness ratio; LAGB = laprascopic adjustable gastric banding; QALY = quality-adjusted life year; RCT = randomized controlled trial; RYGB = Roux-en-Y gastric bypass; SMM = standard medical management; SR = systematic review; T2DM = type 2 diabetes mellitus; UK = United Kingdom; US = United States

APPENDIX 4: Summary Results of the Included Studies

Table 8: Summary estimates reported in Systematic Reviews and Meta-Analyses

Comparison	Follow up	Weight Change	BMI change kg/m^2	Morbidity Control	Safety and Adverse Events	Author Conclusions
DIABETES						
AHRQ[8]						
BS intervention vs. another, MM, or no intervention	1 year	NR MM vs. BS in 1 included RCT: BS patients lost more weight, p<0.001	-5 to -7 MM vs. BS in 1 included RCT: BS patients had a larger decrease in BMI p<0.001	HbA1C as % of total hemoglobin: decrease 2.6 to 3.7 (percentage points) DM2 Resolution • RYGB: 87.2% (≥ 1 yr follow-up) • SG: 50% (≥ 1 yr follow-up) • BPD: 83.5% (≥ 1 yr follow-up) DM2 medication discontinuation: • LABG: 36.4% RYGB: 87.2% (12 to 20 months)	One death, a case of sepsis at 20 months in an LAGB patient. No evidence regarding: all-cause mortality, cardiovascular mortality and morbidity, peripheral arterial disease	Authors concluded that there was moderate strength evidence (based on glucose outcomes) of efficacy for RYGB, LAGB, and SG as treatment for diabetes and IGT in patients with a BMI between 30 kg/m2 and 35 kg/m2 in the short term (up to 2 years). They also concluded that short term adverse events were relatively minor, but that there was insufficient evidence to make conclusions regarding long-term adverse events.
	2 year	MM vs. BS in 2 included RCTs: BS patients lost more weight, p<0.001	-4 to -8 MM vs. BS in 2 included RCTs: BS patients had a larger decrease in BMI, p<0.001	HbA1C as % of total hemoglobin: decrease of 1.8 to 3.1 (percentage points) DM2 medication discontinuation: • RYGB: 87.2% (12 to 24 months)		
	≥5 year	NR	-5.7[a]	HbA1C decrease: NA		
Maggard-Gibbons,[9]						
Surgical vs. Non-Surgical interventions (direct	12 months (one RCT only)	Mean(SD) GBP = -29.4 kg (8.9) GS = -25.1 kg (8.5) MM = -5.4 kg (8.0)	(mean change) GBP = -10.5 GS = -9.0	FBG median, IQR mg/dL GBP = 99 (83-121) GS = 97 (84-114) MM = 120 (97-154)	NR for subgroups – long term adverse events unknown.	Authors concluded that in patients with DM2 and a BMI between 30 and

Table 8: Summary estimates reported in Systematic Reviews and Meta-Analyses						
Comparison	**Follow up**	**Weight Change**	**BMI change kg/m^2**	**Morbidity Control**	**Safety and Adverse Events**	**Author Conclusions**

comparison)		Surgical vs. non surgical: p<0.001	MM = -2.4
			
			Surgical vs. non surgical mean BMI at 12 mo: p<0.001
				Surgical vs. non surgical: p≤0.002
				
				Patients with HbA1C <6.0
				GBP = 21 (42%)
				GS = 18 (37%)
				MM = 5 (12%)
				Surgical vs. non surgical: p≤0.002
				
				Average # DM2 medications
				GBP = 0.3
				GS = 0.9
				MM = 3.0
				Surgical vs. non surgical: p<0.001
						35, BS was associated with more short term weight loss and better glucose outcomes. They also concluded that there was not enough long-term follow-up data to make firm recommendations regarding the procedure.

	24 months (one RCT only)	GB vs. MM between group comparison (Mean, 95% CI): -19.6 (23.8 to 15.2) p<0.001		FBG GB vs. MM between group comparison (Mean, 95% CI): -32.8 (-53.1 to -12.3) p=0.002 Patients with HbA1C <6.2: GB = 24 (80%) MM = 6 (20%) p<0.001 Patients in DM2 remission: GB = 22 (73%) MM = 4 (13%) p<0.001	NR for Subgroups	
Surgical interventions (non-comparative, before/after)	12 to 24 months	NR	Mean change, (95% CI) GBP = -7.5 (-8.8 to -6.2) GB = -4.0 (1 study only) GS = -7.3 (-13.7 to -0.9) BPD = -5.6 (-7.5 to -3.6)	Mean (95% CI) change in HbA1C: GBP: -2.4 (-3.0 to -1.8) GS: -2.8 (-3.6 to -1.9) BPD: -3.1 (-4.2 to -1.9) Mean change (95% CI) Glucose[b] GBP = -74.1 (-96.3 to -51.8) GS = -62.6 BPD = -92.4 (-214.7 to 30.0) Mean change in % patients receiving DM2 medications: GBP = -87.2 (106.9 to 67.5)	NR for subgroups	

Table 8: Summary estimates reported in Systematic Reviews and Meta-Analyses						
Comparison	**Follow up**	**Weight Change**	**BMI change kg/m^2**	**Morbidity Control**	**Safety and Adverse Events**	**Author Conclusions**
				GB = -36.4 BPD = -71.4 DM2 remission or resolution (mean %, SE): GBP = 76.8 (4.3) GS = 56.4 (17.8) BPD = 83.5 (16.5)		
Dixon[11]						
LAGB before/after	12 months	Weighted average EWL: 34.8%	NR	Weighted Average DM2 remission: 52.3% Improved DM2 (but no remission): 16.8% Published studies were more positive	Safety and adverse events specific to DM2 not reported in the included studies.	Authors concluded that there was a lack of high quality studies and long-term outcome data. However, they stated that the current studies provide compelling evidence that LAGB leads to both long- and short-term improvements in DM2 outcomes in obese patients with DM2.
	15 to 24 months	Weighted average EWL: 47%	NR	Weighted Average DM2 remission: 51% Improved DM2 (but no remission): 4% Published and unbublished studies had similar results		
	≥24 months	Weighted average EWL: 44.8%	NR	Weighted Average DM2 remission: 37.6% Improved DM2 (but no remission): 23.1%		
Li[12]						
BS interventions, before/after	Mean 26.8 months	WMD: 17.23 kg loss (95% CI 14.13 to 20.34, $p < 0.00001$)	WMD: -5.18 (95% CI 14.13 to 20.34, $p < 0.00001$)	FBG mean change: - 4.80 mmol/L (95% CI, 3.88–5.71 mmol/L, $p < 0.00001$) HbA1c decrease: 2.59% (95% CI 2.12–3.07%, $p < 0.00001$) Resolution of DM2 (definition 1[c]):	Few severe adverse events, early complications (3.2%) No late (after 30 days) complications reported in any	Authors concluded that for patients with DM2 and BMI BMI < 35 bariatric surgery is both safe and effective and that the long-term metabolic

Table 8: Summary estimates reported in Systematic Reviews and Meta-Analyses						
Comparison	**Follow up**	**Weight Change**	**BMI change kg/m^2**	**Morbidity Control**	**Safety and Adverse Events**	**Author Conclusions**
				66.35% Resolution of DM2 (definition 2[d]): 80%	trials.	benefits can be sustained.
Gill[16]						
Before/after LSG	Mean 13.1±8.1 months	EWL: 47.3%±19.1%	Mean: -11.5	DM2 resolution: 66.2% (26 studies) Improved DM2: 26.9% Stable DM2: 13.1% Resolution or improvement of DM2: 97.1% (16 studies) Resolution, improvement, stable disease DM2: 94.8% PGL change: -63 mg/dL HbA1c % change: -1.7	Adverse events for DM2-only population not reported	Authors concluded that most patients with DM2 who undergo LSG experienced improvement or resolution in their diabetes. They also concluded that LSG may play an important therapeutic role for patients with DM2.
Buschwald[17]						
Before/ after BS (GB, GP, GBP, BPD)	<2 years	EWL: 67.1% (38.2 kg)	NR	Resolution of DM2: 80.2%	Data was scarce and heterogenous. Estimated short term mortality from BS: 0.28%	Authors concluded that the majority of DM2 patients that underwent bariatric surgery had improvements or resolution of both clinical and laboratory manifestations of DM2. They also concluded that the response is more pronounced in patients with greater percentage EWL that is maintained for 2 or more years.
	≥2 years	EWL: 58% (42.9 kg)	NR	Resolution of DM2: 74.6%		
	Overall	EWL: 64.4% (40.6 kg)	NR	Resolution of DM2: 78.2% Resolution or improvement of DM2: 86.6%		

Table 8: Summary estimates reported in Systematic Reviews and Meta-Analyses						
Comparison	**Follow up**	**Weight Change**	**BMI change kg/m^2**	**Morbidity Control**	**Safety and Adverse Events**	**Author Conclusions**
SLEEP APNEA						
Sarkosh, 2013[10]						
Before/after bariatric surgery (RYGB, LAGB, LSG, BPD, MIX)	RYGB: mean 29 months LAGB: mean 34.4 months LSG: 24.7 months BPD: 19 months MIX: 21.8 months	RYGB: Mean EWL%: 75.2±26.8 LAGB: Mean EWL%: 66.8±33.0 LSG: Mean EWL%: 46.1±10.5 BPD: Mean EWL%: 53.7±35.9 MIX: Mean EWL%: 68.3±14.2	NR	RYGB: SA resolution: 73% patients SA improvement: 30% SA improvement or resolution: 79% LAGB: SA resolution: 70.5% SA improvement: 32% SA improvement or resolution: 77% LSG: SA resolution: 72% SA improvement: 51% SA improvement or resolution: 86% LSG: SA resolution: 82.3% SA improvement or resolution: 99% MIX: SA resolution: 63% SA improvement: 31% SA improvement or resolution: 88.5%	NR	Authors concluded that bariatric surgery of any kind was an effective procedure for the relief of sleep apnea in obese patients.
HYPERTENSION, HYPERLIPIDEMIA						
Heneghan[15]						
Before/after bariatric surgery (RYGB, BPD most common)	Mean 34 months	Mean %EWL: 52% RYGB: 65% BPD: 69% LAGB: 42% VBG: 54% SG: 50%	NR	Remitted/resolved hypertension: 68% Remitted/resolved diabetes: 75% Remitted/resolved hyperlipidemia: 71% Change in FBG: -32	CV mortality: BS: 2.1% Control: 2.6% (reported in one study)	The authors concluded that bariatric surgery was beneficial in reducing or eliminating cardiovascular risk factors in obese patients.

Table 8: Summary estimates reported in Systematic Reviews and Meta-Analyses						
Comparison	**Follow up**	**Weight Change**	**BMI change kg/m^2**	**Morbidity Control**	**Safety and Adverse Events**	**Author Conclusions**
Sarkhosh,2012[13]						
Before/after LSG	16.9 months (±9.8)	Mean: 63.3% ±14.8%	-13.1	Resolution of hypertension: 58% (after 12 months) Resolution or improvement of hypertension: 75% Age a negative predictor for resolution of hypertension – younger patients had better resolution of hypertension (p = 0.005) EWL a positive predictor of resolution of hypertension (p = 0.001)	NR	Authors concluded that LSG had a significant effect on the resolution or improvement of hypertension in patients with a BMI >30.
Vest[14]						
Before/after any BS	57.8 months	average 54.2%	NR	Resolution or improvement in hypertension: 52.5% Resolution or improvement in hyperlipidemia: 65.2% Resolution or improvement in DM: 73.2% Effect estimates corrected for publication bias: Hypertension: 0.36 (0.31 to 0.42) Hyperlipidemia: 0.34 (0.28 to 0.40) Diabetes: 0.26 (0.21 to 0.31) (all statistically significant)	NR	Authors concluded that BS was beneficial in reducing cardiovascular risk factors and enhanced future CV health in patients with BMI>30.

BS = bariatric surgery; BPD = biliopancreatic diversion; CI = confidence interval; EWL = excess weight loss; FBG = fasting blood glucose; GB = gastric banding; GBP = gastric bypass; GP = gastroplasty; HbA1C = hemoglobin A1C; LAGB = laparoscopic adjustable gastric banding; LSG = laparoscopic sleeve gastrectomy; MM = medical management; MIX = mixed surgical group; PGL = plasma glucose level; RYGP = roux-en-y gastric bypass; SA = sleep apnea; SG = sleeve gastroscopy; VBG = vertical banded gastroscopy; WMD = weighted mean difference

[a]Data from a single study examining 29 LAGB studies

[b]not specified

[c] normal FPG (<100 mg/dl), a normal HbA1c (<6%) and no need for diabetic medications

[d] HbA1c <7% and no need for diabetic medications

Table 9: Summary of the Included Guidelines		
Subgroup	**Strength of Recommendation**	**Recommendation**
Runkel,2011[18]		
DM2	Grade C (considered "may do")	"type II diabetes mellitus is held to be an independent indication criterion for patients whose BMI lies between 30 and 35 kg/m^2" "Surgery may also be considered in patients with type 2 diabetes mellitus and a BMI of 30–35 kg/m^2. These well selected cases should be enrolled into trials."
Other Comorbidities	Grade A (considered "must do")	"In patients with a BMI of 35–40 kg/m2 and with one or more obesity-associated disorders (e.g., type 2 diabetes mellitus, coronary heart disease, etc.) is also a candidate for surgical treatment if conservative treatment has failed or appears futile."
Yermilov, 2009[20]		
DM2	Not given	Bariatric surgery is appropriate for patients with DM2 and: • With BMI ≥40, aged 19–55 regardless of DM2 severity • For patients 65+ years with BMI ≥40, including, HbA1c >9, regardless of therapy, or 7–9 on maximal medical therapy • 19–64 years with BMI 34–39 regardless of DM2 severity • 65+ years with BMI 34–39 with all DM2 severity levels except HbA1c 7–9, not on maximal therapy. • 19 – 64 years, BMI 32–34, severe category of diabetes (HbA1c >9, on maximal medical therapy) Unclear if bariatric surgery is appropriate for patients who have severe DM2, are aged 19-55, with BMI ≤30 to 31.
Hypertension	Not given	Bariatric Surgery is appropriate for patients with hypertension and: • With BMI ≥40, aged 19–55 regardless of hypertension severity • For patients 65+ years and BMI ≥40, regardless of treatment • 19–64 years with BMI 34–39 regardless of hypertension severity • 65+ years with BMI 34–39 and severe hypertension (hypertension despite maximal treatment) Unclear if bariatric surgery is appropriate for patients who have severe hypertension, are aged 19-55, with BMI ≤30 to 31.
Dyslipidemia	Not given	Bariatric Surgery is appropriate for patients with dyslipidemia and: • With BMI ≥40, aged 19–55 regardless of lipid dyslipidemia severity • For patients 65+ years and BMI ≥40, regardless of treatment • 19–64 years with BMI 34–39 regardless of dyslipidemia severity Unclear if bariatric surgery is appropriate for patients who have severe dyslipidemia,

Table 9: Summary of the Included Guidelines		
Subgroup	**Strength of Recommendation**	**Recommendation**
		are aged 19-55, with BMI ≤30 to 31.
Sleep Apnea	Not given	Bariatric Surgery is appropriate: • With BMI ≥40, aged 19–55 regardless of sleep apnea severity • For patients 65+ years, BMI ≥40, and severe to moderate sleep apnea • 19–64 years with BMI 34–39 regardless of sleep apnea severity • 65+ years with BMI 34–39 and moderate to severe sleep apnea Unclear if bariatric surgery is appropriate for patients who have severe sleep apnea, are aged 19-55, with BMI ≤30 to 31.

Table 10: Summary of findings of included Cost-effectiveness analyses		
First Author, Year	**Main Study Findings**	**Author Conclusions**
Pollock, 2013[21]	• Surgical management more costly, more effective • ICER LAGB vs. MM £3,602/QALY • Assuming Willingness to Pay threshold £20,000/QALY, model projected 100% likelihood of cost-effectiveness for LAGB over MM • Only the worst-case sensitivity analysis (where ICER was £36,777/QALY) was not cost-effective	From the UK healthcare payer perspective, LAGB considered cost-effective in patients who are obese and have DM2.
Picot, 2012[22]	CE for BMI ≥30 and <40 with DM2: • Surgical management more costly, more effective • ICER LAGB vs. MM o 2 years £20,159 o 5 years £4,969 o 20 years £1,634 • 1-way sensitivity analyses, least favourable ICERs associated with short timeline. • At 20 yrs, assuming willingness to pay threshold £20,000/QALY, LAGB cost effective over MM 59% of time. Threshold of £30,000/QALY yielded 100% chance of cost effectiveness.	From the UK healthcare payer perspective, bariatric surgery is likely cost-effective for patients with BMI ≥30 and <40 and DM2.
Hoerger, 2010[23]	Bariatric surgery was not cost-saving. Patients with newly established diabetes base-case ICER vs. MM: • GBP: US$7,000/QALY • GB: US$11,000/QALY Patients with established diabetes base-case ICER vs. MM: • GBP: US$12,000/QALY • GB: US$13,000/QALY Sensitivity analyses with lower BMI (30 –34 kg/m^2 instead of ≥35) doubled the ICER.	Both GBP and GB are relatively cost-effective, with ICER ranging $7,000 to $13,000/QALY. Authors stated this is well below the established willingness to pay threshold of $50,000/QALY.
Klarenbach, 2010[1]	ICER RYGB vs. MM DM2: • CAN$12,701/QALY at 10 years • CAN$4,151/QALY at 20 years	From a Canadian health payer perspective, RYGB more effective, less costly over the lifetime horizon in patients with DM2.

Table 10: Summary of findings of included Cost-effectiveness analyses		
First Author, Year	**Main Study Findings**	**Author Conclusions**
	• RYGB dominant in lifetime horizon. ICER RYGB vs. MM – other comorbidities, lifetime horizon: • Hypertension: CAN$8,659/QALY • Hyperlipidemia: CAN$7,811/QALY • Sleep apnea: $5,246/QALY Conclusions not sensitive to changes in perioperative risk of death.	
Anselmino, 2009[24]	Austria (5 year ICER) AGB vs. CT: -€2,861/ QALY GBP vs. CT: -€1,447 Italy (5 year ICER) AGB vs. CT: -€1,077/QALY GBP vs. CT: -€1,246/QALY Spain (5 year ICER) AGB vs. CT: €1,456/QALY GBP vs. CT: €2,664/QALY	AGP and GBP are cost saving over CT in both Austria and Italy and increase costs in Spain. At a willingness to pay threshold of €30,000/QALY, AGP and GBP are cost-effective in all three countries, even when worst-case scenarios were run.
Ikramuddin, 2009[25]	Base Case RYGB vs. MM (35 year ICER): US$21,973/QALY 10 year ICER: $US122,001/QALY 84% probability of being CE at willingness to pay at or below US$50,000/QALY	At the base-case scenario, RYGB provides good value for money over medical management. In most scenarios, the ICER remained below US$50,000/QALY.
Keating, 2009[26]	Bariatric Surgery vs. CT: surgery was cost saving of AUD$ 2,400 • 95% CI dominant to AUD$48,400 per QALY for ICER Probability of surgery being dominant in all cases: 54% Probability of surgery being cost-effective in all cases: 98% Threshold analysis: Surgery is cost effective if mean duration of remission is 2 years; is dominant if 10 years	Bariatric surgery is cost-saving in obese Australian patients with DM2.
Picot, 2009[27]	ICER AGB vs. MM: • 2 years: £18,930/QALY • 5 years: £4,580/QALY	2 years • At a willingness to pay threshold of £20,000/QALY, bariatric surgery is CE 2.5% of the time

Table 10: Summary of findings of included Cost-effectiveness analyses		
First Author, Year	**Main Study Findings**	**Author Conclusions**
	• 20 years: £13,67/QALY Sensitivity Analyses: • Least favourable ICERs associated with short time horizon (range £19,000/QALY to £35,000/QALY) • More favourable ICERs associated with longer time horizon (range £1,300/QALY to £10,000/QALY) Results generally robust to changes in assumptions.	• At a willingness to pay threshold of £30,000/QALY, bariatric surgery is CE 50.6% of the time <u>20 years</u> • Surgical management of obesity in obese patients with DM2 is cost-effective at both £20,000/QALY and £30,000/QALY 100% of the time.

AGB = adjustable gastric bypass; AUD = Australian dollar; DM2 = type 2 diabetes mellitus; CAD = Canadian dollar; CT = conventional therapy; ICER = incremental cost-effectiveness ratio; LAGB = laparoscopic adjustable gastric banding; MM = medical management; QALY = quality adjusted life year; RYGB = Roux-en-Y gastric bypass; UK = United Kingdom; US = United States