NCCHTA

21 January 2009

Protocol for HTA Technology Assessment Report no 08/06
February 2008 (received 08/05/08)

1 Title of the project: The clinical-effectiveness and cost-effectiveness of bariatric surgery for obesity: a systematic review and economic evaluation.

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3 Plain English Summary

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. To decide whether someone is overweight or obese their body mass index (BMI) can be calculated by taking the weight of a person in kilograms and dividing by the square of their height in meters (kg/m^2). People with a BMI of 30 or more are defined as being obese, those with a BMI of 40 or more as morbidly obese. Currently in England about 38% of people aged 16 or over are overweight, 24% are obese and about 2.1% are morbidly obese. In the 11-15 years age group the prevalence of obesity is about 20%. The proportion of people who are obese is predicted to rise in the future.

As people become overweight and then continue to gain weight they increase their risk of developing health problems. If they lose weight some of the health problems associated with being obese may improve or even disappear completely. Sometimes an operation may be suggested. However, in current NICE guidelines an operation is only recommended for people who:

- are seriously obese
- have tried all the other ways of losing weight without success
- have already been treated by a specialist obesity team.

The main types of operation for weight loss involve either making the stomach smaller, or either shortening or bypassing part of the intestine so that less food can be absorbed, or a combination of these approaches.

There are several different kinds of operation that can be carried out, and it is not clear which one is the safest and most effective. This study will build on and update an earlier review of

the different kinds of operation for weight loss. It will systematically summarise the results of studies which have compared different kinds of weight loss surgery and other methods of losing weight such as diet, anti-obesity drugs and exercise. The report will also include a systematic review of cost-effectiveness studies and an economic evaluation. The economic evaluation will compare the costs and benefits of the different types of weight loss surgery and other methods of losing weight to find out whether they represent good value for money from the perspective of the NHS and personal social services.

4 Decision problem

The aim of this health technology assessment is to assess the clinical effectiveness and cost-effectiveness of bariatric surgery in the obese.

Bariatric surgery for people with morbid obesity was assessed in 2002[1]. In addition a Cochrane review (which did not contain an economic evaluation) based on this assessment was published in 2003 and this was updated in 2005.[2]

This health technology assessment will update the original assessment whilst also broadening the scope to include people who are obese as well those who are morbidly obese. Since NICE guidelines[3] do not rule out surgical intervention for obese young people this assessment will seek evidence on this population group.

4.1 Background to Bariatric Surgery for Obesity

Obesity

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. The most commonly used measure for classifying overweight and obesity is the Body Mass Index (BMI). This is a simple index of weight-for-height that is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2). Obesity in adults is most commonly defined as a BMI of over 30, and severe or morbid obesity as a BMI of over 40 (Table 1). BMI (adjusted for age and gender) is also recommended by the NICE guideline on obesity[3] as a practical estimate of overweight in children and young people, but the guideline points out that this needs to be interpreted with caution because it is not a direct measure of adiposity (the amount of body fat). For children and young people overweight and obesity are not defined according to a particular BMI. The NICE obesity guideline instead recommends that tailored clinical intervention should be considered for children with a BMI at or above the 91st centile and assessment of comorbidity should be considered for children with a BMI at or above the 98th centile.

Table 1: The International Classification of adult underweight, overweight and obesity according to BMI[4,5]

Classification	**BMI(kg/m^2)**	**Risk of comorbidities**
Underweight	<18.5	Low (but risk of other clinical problems increased)
Normal range	18.50-24.99	Average
Overweight	**≥25.00**	
Pre-obese	25.00 - 29.99	Increased
Obese	**≥30.00**	
Obese class I	30.00 - 34-99	Moderate
Obese class II	35.00 - 39.99	Severe
Obese class III (morbid obesity)	≥40.00	Very severe

Epidemiology

The World Health Organisation's (WHO's) projections indicated that globally in 2005 approximately 1.6 billion adults (age 15+) were overweight and at least 400 million adults were obese.[6] In England in 2006 the prevalence of overweight in people aged 16 and over was 38% (approximately 15.4 million people), with 24% obese (approximately 9.8 million people).[7] The prevalence of morbid obesity is low at 2.1% (just under 863,000 people) with women being more likely to be morbidly obese than men (3% of women versus 1% of men). In the 11-15 years age group the prevalence of obesity in 2005 was very similar in boys and girls at 20.5% and 20.6% respectively and in general the proportion of children who are obese increases with age.[8]

The prevalence of obesity is predicted to rise in the future. WHO has projected that by 2015 more than 700 million adults will be obese. In the UK the Foresight programme provides visions of the future based on robust science. The Foresight project "Tackling Obesities: Future Choices" produced a report made up of a number of documents. The report forms a long-term vision of how a sustainable response to obesity can be delivered in the UK over the next 40 years. The modelling section of the Foresight Report predicts that in England, if current trends persist, 36% of men and 28% of women aged 21 to 60 will be obese in 2015.[9] Predicting trends in morbid obesity is more problematic. The Foresight modelling projection to 2050 suggests figures of 1% for males and 4% for females.[9] In contrast a different Foresight project output has estimated that the proportion of morbidly obese English males and females will reach nearly 3% and 6% respectively in 2030.[10] For children the Foresight modelling project predicts that the proportion of those who are obese in the under-20 age group, will rise to approximately 10% by 2015. By 2025, around 14% of the under-20s will be obese, and it is predicted that by 2050 this will be around 25%.[9]

Health consequences

Obesity can cause a variety of adverse health consequences. An increased risk of health problems starts when someone is only very slightly overweight, and the likelihood of adverse health consequences increases as someone becomes more and more overweight.[6] The predominant serious health consequences associated with overweight and obesity include Type 2 diabetes, cardiovascular disease (mainly heart disease and stroke), musculoskeletal disorders such as osteoarthritis, and certain cancers (endometrial, breast and colon) (Table 2).

Table 2 Health Problems associated with obesity[5]

Greatly increased risk (relative risk* much greater than 3)	**Moderately increased risk (relative risk* 2-3)**	**Slightly increased risk (relative risk 1-2)**
Type 2 diabetes (Non-insulin dependent diabetes mellitus)	Coronary heart disease	Cancer (breast cancer in postmenopausal women, endometrial cancer, colon cancer)
Gallbladder disease	Hypertension	Reproductive hormone abnormalities
Dyslipidaemia	Osteoarthritis (knees)	Polycystic ovary syndrome
Insulin resistance	Hyperuricaemia and gout	Impaired fertility
Breathlessness		Low back pain due to obesity
Sleep apnoea		Increased risk of anaesthesia complications
		Fetal defects associated with maternal obesity

* Relative risk values are approximate

Benefits of weight loss

A systematic review of the long-term effects of obesity treatments on body weight, risk factors for disease, and disease[11] found that weight loss from surgical and non-surgical interventions for people suffering from obesity was associated with decreased risk of development of diabetes, and a reduction in low-density lipoprotein cholesterol, total cholesterol and blood pressure, in the long term. A further systematic review of the long-term weight loss effects on all cause mortality in overweight/obese populations[12] concludes that there is some evidence that intentional weight loss has long-term benefits on all cause mortality for women and more so for people with diabetes. However the long-term effects for men are not clear.

4.2 Place of the intervention in the treatment pathway(s)

NICE guidelines[3] state that intensity of management for overweight and obesity will depend on the level of risk of health problems and the potential to gain benefit from weight loss. In the early stages of overweight, advice on what constitutes a healthy lifestyle and the healthy weight for the particular individual should be provided within the primary care setting. As the degree of overweight increases, and depending on the presence or absence of comorbidities, intensity of management would increase to include diet and exercise, then a consideration of a prescription for anti-obesity drugs. Surgery is usually considered a last resort intervention. In the current NICE guidelines[3] bariatric surgery is recommended as a treatment option for adults with obesity if all of the following criteria are fulfilled:

− they have a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 and other significant disease (for example, Type 2 diabetes or high blood pressure) that could be improved if they lost weight

− all appropriate non-surgical measures have been tried but have failed to achieve or maintain adequate, clinically beneficial weight loss for at least 6 months

− the person has been receiving or will receive intensive management in a specialist obesity service

− the person is generally fit for anaesthesia and surgery

− the person commits to the need for long-term follow-up.

For adults with a BMI of more than 50 kg/m^2 bariatric surgery is also recommended as a first-line option (instead of lifestyle interventions or drug treatment) if surgical intervention is considered appropriate.

NICE guidelines[3] do not rule out surgical intervention in young people. Whilst it is acknowledged that surgical intervention is not generally recommended in children or young people the guidelines state that bariatric surgery may be considered for young people only in exceptional circumstances, and if they have achieved or nearly achieved physiological maturity.

4.3 Types of Bariatric Surgery for Obesity

The aim of surgery is to reduce weight and maintain any loss through restriction of intake or malabsorption of food or both. It is hoped that as a consequence eating behaviour is modified, with patients consuming smaller quantities of food more slowly. Surgery for morbid obesity is a major surgical intervention with a risk of significant early and late morbidity and of perioperative mortality. Our review will focus on the principal types of surgical procedure that are in current use, these are summarised below.

Gastric bypass (Roux-en-Y and resectional)

These procedures combine restriction and malabsorption techniques, creating both a small gastric pouch and an intestinal bypass that prevents the patient from absorbing all they have eaten.[1] Complications associated with gastric bypass include failure of the staple partition, leaks at the junction of the stomach and small intestine, delayed gastric emptying either spontaneously or secondary to a blockage of the efferent limb. Other complications following

surgery include vomiting, intestinal obstruction (functional or mechanical), wound hernias, anaemia due to lack of impaired absorption of iron or vitamin B12 and calcium deficiency (all are overcome by supplements). Dumping syndrome can also occur (an adverse event caused by eating refined sugar symptoms of which include rapid heart rate, nausea, tremor, faint feeling and diarrhoea).

Vertical banded gastroplasty

During this procedure the stomach is partitioned, using surgical staples, to create a small segment at the top of the stomach which is partially separated from the remainder of the stomach, with only a small gap (stoma) remaining. The intention is to cause the person to have the sensation of fullness from a limited intake of food. This procedure has the advantage of being a restrictive procedure with no malabsorption component or dumping but weight regain is common. Complications are relatively rare with a low postoperative mortality rate, although revision rates requiring further surgical intervention are often high. Specific complications include bolus obstruction and there are few instances of anaemia or calcium or vitamin deficiencies. Other complications include leakage, stenosis, ulcer, incisional hernia, wound infection, staple line disruption, pouch dilation and band erosion. It is a reversible procedure.

Gastric banding

Gastric banding is the least invasive of the purely restrictive bariatric surgery procedures. It limits food intake by placing a constricting ring completely around the top end (fundus) of the stomach, below the junction of the stomach and oesophagus. While early bands were non-adjustable, those used currently incorporate an inflatable balloon within their lining to allow adjustment of the size of the stoma to regulate food intake. Increasingly, gastric bands are placed through laparoscopic surgery, decreasing time spent in hospital. Adjustment is undertaken without the need for surgery by adding or removing an appropriate material (for example saline) through a subcutaneous access port. As a restrictive procedure, gastric banding avoids the problems associated with malabsorptive techniques. Complications include splenic injury, oesophageal injury, wound infection, band slippage, band erosion (or migration), reservoir deflation/leak, persistent vomiting, failure to lose weight and acid reflux. Some studies have documented a high need for revisional or band-removal surgery as a result of complications.[13]

Biliopancreatic diversion (Scopinaro's procedure) and duodenal switch

Biliopancreatic diversion and duodenal switch are primarily malabsorptive procedures. The duodenal switch is a US adaptation of the biliopancreatic diversion. Both procedures involve the removal of part of the stomach (a limited (sleeve) gastrectomy) and bypassing part of the small intestine (the malabsorptive component). The gastric pouch which is created is larger than that of gastric bypass or the restrictive procedures (100 to 150 ml) therefore allowing larger meals, and patients remain on a less restricted diet than would be the case following gastric bypass. The procedures avoid leaving a non-functioning intestinal segment by dividing the intestine into a long enteric limb joining a long biliopancreatic limb to form a common channel 50 to 150 cm from the ileocecal valve. This causes fewer liver problems and avoids the toxic problems associated with the old jejunoileal bypass procedure.[14] Side effects include loose stools, stomal ulcers, offensive body odour and foul smelling stools and flatus. Serious complications include anastamotic leak and anastomotic ulceration, protein malnutrition, hypoalbuminemia, anaemia, oedema, asthenia (lack of energy) and alopecia (hair loss).[15,16] As a result of malabsorption, patients usually need calcium and vitamin supplements and follow-up lifelong. In an attempt to overcome these complications, several variants of the procedure have been developed.

4.4 Relevant comparators

The remit of this review has been broadened since the original assessment. In addition to including morbidly obese people, this updated assessment will also include obese people. Since surgery is usually considered a last resort intervention for people who are morbidly obese much of the published evidence reports comparisons between one type of bariatric surgery and another. However, there are examples of RCTs and controlled studies which have compared surgical to non-surgical interventions in morbidly obese people, such as dietary interventions or the most appropriate conventional or medical management.[1,2] Comparisons of surgical versus non-surgical interventions may be more common when the population under consideration is obese people. The comparators included in this review may therefore include alternative types of bariatric surgery, dietary, exercise and pharmacological (e.g. orlistat, sibutramine, and rimonabant) interventions either individually, or in combination e.g. diet and exercise.

4.5 Population and relevant sub-groups

The main population under consideration will be

- adults who meet the current NICE guidelines for bariatric surgery[3], i.e. adults with a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 with other significant disease (for example, Type 2 diabetes or high blood pressure) that could be improved if they lost weight.

However, the review will also seek evidence on two additional population groups:

- obese adults (BMI of 30 or over). Adults with a BMI of under 35 or a BMI of 35-40 and no comorbidities would not currently meet the NICE criteria for bariatric surgery. However, for some adults with a BMI in the 30-40 range the benefits of bariatric surgery may outweigh the potential harms. Some research investigating bariatric surgery for people with mild to moderate obesity has already been published[17,18] such evidence will be assessed for inclusion in the review.
- Since the NICE guidelines[3] do not rule out surgical intervention in young people evidence will be sought on the use of bariatric surgery for obesity in this population group.

4.6 Outcomes

The clinical outcomes which will be reported will match those of the original TAR, namely measures of weight change, quality of life, peri- and post-operative mortality and morbidity, change in obesity-related comorbidities, and cost-effectiveness. It will be necessary to identify the resource implications of interventions and comparators e.g. time in surgery, counselling time with dietitian etc, since these factors will help to inform the economic model. It is anticipated that the principle outcome of the economic model will be expressed in terms of incremental cost per quality adjusted life year (QALY) gained.

4.7 Key factors to be addressed (e.g. further considerations, problematic factors)

Problematic factors are likely to be a limited quantity of published research on both adults with a lower BMI (the BMI 30-35 in particular) and on adolescents. The impact of this is that it may not be possible to model cost-effectiveness outcomes for these two groups.

There is likely to be a limited number of studies reporting health state utility for obesity or BMI, based on responses to the EQ-5D. As a result, utility weights obtained using other approaches (alternative generic instruments such as the SF-36/SF-6D as well as standardised methods such as the standard gamble or time trade off) will need to be considered. Appropriate methods to synthesise valuations estimated using different instruments and analytical methods will need to be considered. In addition, sensitivity analyses on health state valuations will need to consider uncertainty arising from the variation in methods used to derive those valuations and the settings in which they occurred, in addition to uncertainty over the parameter values.

5 Report methods for the synthesis of clinical- and cost-effectiveness evidence

A review of the evidence for clinical-effectiveness and cost-effectiveness will be undertaken systematically following the general principles outlined in CRD Report Number 4 (2nd Edition) 'Undertaking Systematic Reviews of Research on Effectiveness'.[19]

5.1 Search strategy

The search strategies will be devised and tested by an experienced information scientist. The strategies will be designed to identify (i) clinical-effectiveness studies reporting on comparisons between different bariatric surgical techniques, and comparisons between bariatric surgery and non-surgical interventions for obesity; and (ii) studies reporting on the cost-effectiveness of different bariatric surgical techniques, and comparisons between bariatric surgery and non-surgical interventions for obesity.

The search strategy will involve searching of the following electronic databases: MEDLINE; EMBASE; PreMedline In-Process & Other Non-Indexed Citations; The Cochrane Library including the Cochrane Systematic Reviews Database, Cochrane Controlled Trials Register, DARE, NHS EED and HTA databases; Web of Knowledge Science Citation Index (SCI); Web of Knowledge ISI Proceedings; PsycInfo; CRD; Biosis (see Appendix, 11.1).

As described above (section 4), this work will update a previous assessment[1] but the updated work will include obese people as well as morbidly obese people. The searches for the previous assessment were carried out in 2001. Clinical effectiveness searches were then carried out again in 2004 to inform the Cochrane review which was updated in 2005. The results of these searches will help to inform our review. In particular we will check the 2001-2004 search results for studies that were excluded because the patients were not morbidly obese, but which would meet the criteria for this updated review that will include obese people. New searches will be conducted for clinical-effectiveness evidence published since 2004. For the cost-effectiveness section searches will be carried out from 2001. Searches for other evidence to inform cost-effectiveness modelling will be conducted as required (see Section 6.1) and may include a wider range of study types (including non-randomised studies and cost effectiveness analyses of pharmaceuticals for weight reduction).

All searches will be updated when the draft report is under review, prior to submission of the final report.

Bibliographies of related papers will be assessed for relevant studies.

Members of the Expert Advisory Group will be asked to review the adequacy of the searches and to indicate whether they are aware of any additional published or unpublished evidence.

5.2 Inclusion and exclusion criteria

5.2.1 Population

Inclusion criteria:

- Adult patients fulfilling the standard definition of obese, i.e. people with a body mass index (BMI) of 30 kg/m^2 or over.
- Young people who fulfil the definition of obesity for their age, sex and height.
- Where data are available clinical-effectiveness and cost-effectiveness will be reported separately for patients who meet current NICE guidelines for bariatric surgery, those with a lower BMI who would not currently meet the NICE criteria for bariatric surgery, and young people.

Exclusion criteria:

- Adults with a BMI under $30kg/m^2$

5.2.2 Intervention

Inclusion criteria

- Open and laparoscopic bariatric surgical procedures in current use. The procedures likely to be included are vertical banded gastroplasty, gastric banding (including adjustable gastric banding), biliopancreatic diversion (including biliopancreatic diversion with duodenal switch), gastric bypass and sleeve gastrectomy.

5.2.3 Comparators

Inclusion criteria

- Surgical procedures in current use will be compared with one another.
- Open surgery will be compared with laparoscopic surgery for the same procedure.
- Surgical procedures in current use will be compared to non surgical interventions. These non-surgical interventions may include drugs such as orlistat, sibutramine and rimonabant, dietary interventions, exercise, and combinations of non-surgical interventions such as diet and exercise.

Exclusion criteria:

- Comparisons of variations in technique for a single type of surgical procedure

5.2.4 Outcomes

Inclusion criteria

- Studies must have reported on at least one of the following outcomes following a minimum of 12 months of follow-up: weight change; quality of life; change in obesity related co-morbidities.
- Data will also be extracted on peri- and post-operative mortality and morbidity, revision rates for surgical procedures, change in obesity related co-mobidities, and cost-effectiveness.

Exclusion criteria:

- Studies will not be included if they have only reported short term outcomes (less than 12 months).

5.2.5 Types of studies

Inclusion criteria

- Randomised controlled trials (RCTs) will be included. For the comparisons of surgical procedures with non-surgical procedures it is likely that few or no RCTs will be found, controlled clinical trials and prospective cohort studies (with a control cohort) will therefore also be eligible for inclusion.
- For the systematic review of cost-effectiveness study types will include full cost-effectiveness analyses, cost-utility analyses, cost-benefit analyses and cost-consequence analyses.
- Studies published as abstracts or conference presentations will only be included if sufficient details are presented to allow an appraisal of the methodology and the assessment of results to be undertaken.

Exclusion criteria:

- Case series and case studies
- Narrative reviews, editorials and opinions

5.3 Reference screening, Data extraction, and Quality Assessment

5.3.1 Reference screening strategy

- Titles and abstracts identified by searching will be examined for inclusion, according to the inclusion/exclusion criteria detailed above, by two reviewers independently. Disagreements will be resolved by consensus or by recourse to a third reviewer where necessary.

- For studies which appear potentially relevant on title or abstract, full papers will be requested for further assessment. All full papers will be screened independently by two reviewers and a final decision regarding inclusion will be agreed. Any disagreements will be resolved by discussion, with involvement of the third reviewer where necessary.

5.3.2 Data extraction strategy

- Data will be extracted by one reviewer using a standardised data extraction form (see Appendix, 11.2). Extracted data will be independently checked by a second reviewer. Discrepancies will be resolved by discussion, with involvement of another reviewer when necessary.

5.3.3 Quality assessment strategy

- Cohort studies will be assessed using criteria recommended by the NHS CRD (University of York)[19]
- RCTs will be assessed using the Cochrane criteria for judging risk of bias.[20] These criteria include consideration of the following factors:
    1. Sequence generation
    2. Allocation concealment
    3. Blinding of participants, personnel and outcome assessors
    4. Incomplete outcome data
    5. Selective outcome reporting
    6. Topic-specific, design-specific or other potential threats to validity
- Economic evaluations will be assessed using the critical appraisal checklist for economic evaluations proposed by Drummond and colleagues.[21]
- The checklist for assessing good practice in decision analytic modelling will be used for critically appraising any decision models identified.[22]

5.4 Methods of data analysis/synthesis

- Clinical-effectiveness and cost-effectiveness data will be tabulated and discussed in a narrative review.
- If clinical-effectiveness data are of sufficient quantity, quality and homogeneity, a meta-analysis will be performed to estimate a summary measure of effect on relevant outcomes based on intention to treat analyses. If a meta-analysis is appropriate it will be performed using Review Manager (RevMan) software.

6.0 SHTAC economic model

6.1 Evidence to inform the economic model

The inclusion and exclusion criteria for evidence required to inform the economic model will be identical to the criteria for the systematic review of clinical-effectiveness, with the following exceptions

- The cost-effectiveness model will focus on the surgical procedures identified in the clinical-effectiveness review as being those that are clinically effective and in current use. These will be further restricted to those that are in widespread current use within the UK NHS if necessary.
- Searches for other evidence to inform cost-effectiveness modelling (for example long-term cohort studies to obtain parameter estimates for the comparator arm of the model (non-surgical treatment), studies assessing HRQoL in obese people, studies estimating the relationship between improvements in obesity-related risk factors and the associated potential changes in morbidity and mortality), will be conducted as required and may be drawn from the wide range of sources (such as non-randomised studies and the cost-effectiveness analyses of pharmaceuticals for weight reduction).

6.2 Economic modelling

A new economic evaluation will be carried out, from the perspective of the UK NHS and Personal Social Services (PSS), using a decision analytic modelling approach. Model structure will be determined on the basis of research evidence and clinical expert opinion of:

- The biological disease process (i.e. knowledge of the natural history of the disease);
- The main diagnostic and care pathways for patients in the UK NHS context (both with and without the intervention(s) of interest); and
- The disease states or events which are most important in determining patients' clinical outcomes, quality of life and consumption of NHS or PSS resources.

Where possible the incremental cost-effectiveness of each intervention will be estimated in comparison with other surgical procedures, as well as the non-surgical comparator(s) for adults meeting the current NICE criteria for bariatric surgery. Cost effectiveness will be estimated in terms of incremental cost per quality adjusted life year (QALY) gained. Cost-effectiveness modelling of bariatric surgery for adults with a lower BMI than suggested by current NICE criteria, and bariatric surgery for obese young people will only be considered if sufficient data to inform the cost-effectiveness model is available.

Parameter values will be obtained from relevant research literature, including the systematic review of clinical and cost-effectiveness. Where parameter estimates are not available from good quality published studies data may be obtained from lower quality evidence sources or expert clinical opinion. Sources for parameters will be stated clearly. A specific systematic literature search will be conducted for publications reporting health-related quality of life and/ or health state utility associated with obesity.

Resource use will be specified from the perspective of the NHS and PSS and will be valued using appropriate NHS[23] and PSS[24] reference costs. Where national reference costs are not appropriate, unit cost estimates will be extracted from published work. If insufficient data are retrieved from published sources, costs may be obtained from individual NHS Trusts or groups of Trusts.

The simulated population will be defined on the basis of evidence about the characteristics of the UK adult population undergoing bariatric surgery. Simulated populations of (i) adult patients with a lower BMI who do not meet NICE criteria for bariatric surgery, and (ii) young people will only be defined separately if good quality effectiveness, resource use, and cost data are available for these groups.

If data allow, the time horizon of our analysis will be a patient's lifetime in order to reflect the chronic nature of the disease. Alternatively, the base case analysis will be based on best available data, with lifetime horizon explored in a scenario analysis. Both cost and QALY will be discounted at 3.5%.

Analysis of uncertainty will focus on cost-utility. Uncertainty will be explored through both one-way sensitivity analysis and probabilistic sensitivity analysis (PSA) if the modelling approach permits this. If PSA is undertaken the outputs will be presented both as plots on the cost-effectiveness plane and cost-effectiveness acceptability curves.

7 Advisory Group

The advisory group will be representative of potential users of the review from different professional backgrounds and opinions. We will look to invite people who are academics, clinicians, health economist/methodologists, and patient group representatives to provide expert advice to support the project. The advisory group will be asked to provide comments on a version of the protocol and of the final report, as well as advising on the identification of

relevant evidence. All members of the advisory group will be asked to register competing interests and to keep the details of the report confidential.

8 Competing interests of authors

There are no competing interests.

9 Timetable/milestones

Progress report to be submitted to NCCHTA – July 2008
Assessment Report to be submitted to NICE/NCCHTA – September 2008

10 References

1. Clegg AJ, Colquitt J, Sidhu MK, Royle P, Loveman E, Walker A. The clinical effectiveness and cost-effectiveness of surgery for people with morbid obesity: a systematic review and economic evaluation. *Health Technology Assessment (Winchester, England)* 2002;6:1-153.

2. Colquitt J, Clegg A, Loveman E, Royle P, Sidhu MK. Surgery for morbid obesity. *Cochrane Database Syst Rev* 2005;CD003641.

3. National Institute for Health and Clinical Excellence. Obesity - Guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children. London: The Stationary Office; 2006. Clinical Guideline 43

4. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser* 1995;854:1-452.

5. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* 2000;894:i-253.

6. World Health Organisation. Overweight and Obesity. Factsheet no.311. 2006.

7. Rachel Craig and Jennifer Mindell eds. Health Survey for England 2006. Latest trends. A survey carried out for The Information Centre. 2006.

8. National Statistics TIC. Statistics on Obesity, Physical Activity and Diet: England, January 2008. 2008.

9. McPherson K, Marsh T, Brown M. Foresight. Tackling Obesities: Future Choices - Modelling Future Trends in Obesity and the Impact on Health. 2nd Edition. 2007.

10. Lobstein T, Leach R. Foresight. Tackling Obesities: Future Choices – International Comparisons of Obesity Trends, determinants and responses – Evidence review. 2007.

11. Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC *et al*. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. *Health Technology Assessment* 2004;8:1-194.

12. Poobalan AS. Long-term weight loss effects on all cause mortality in overweight/obese populations. *Obesity Reviews* 2007;8:503-13.

13. Lee CW, Kelly JJ, Wassef WY. Complications of bariatric surgery. *Current Opinion in Gastroenterology* 2007;23:636-43.

14. Buchwald H. Consensus conference statement bariatric surgery for morbid obesity: health implications for patients, health professionals, and third-party payers. *Surg Obes Relat Dis* 2005;1:371-81.

15. Scopinaro N, Adami GF, Marinari GM, Traverso E, Camerini G, Baschieri G *et al*. Long-term results of biliopancreatic diversion in the treatment of morbid obesity. *Acta Chir Austriaca* 1998;30:166-71.

16. Jung RT, Cuschieri A. Obese patients. In: Cuschieri A, Steele RJC, Moosa AR, editors. Essential Surgical Practice-Volume 1 (4th Edition) Butterworth Heinemann 2000. p.227-40.

17. Parikh M, Duncombe J, Fielding GA. Laparoscopic adjustable gastric banding for patients with body mass index of <or=35 kg/m2. *Surgery for Obesity & Related Diseases* 2006;2:518-22.

18. O'Brien PE, Dixon JB, Laurie C, Skinner S, Proietto J, McNeil J *et al*. Treatment of mild to moderate obesity with laparoscopic adjustable gastric banding or an intensive medical program: a randomized trial. *Annals of Internal Medicine* 2006;144:625-33.

19. CRD. Undertaking Systematic Reviews of Research on Effectiveness. York: Centre for Reviews and Dissemination; 2001. No. 4

20. Cochrane Collaboration. Assessing risk of bias in included studies. In: Higgins J, Altman D, editors. Cochrane Handbook for Systematic Reviews of Interventions 2007.

21. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. *BMJ* 1996;313:275-83.

22. Phillips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R *et al*. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess* 2004;8:1-172.

23. Department of Health. NHS Reference Costs 2006-2007. Department of Health . 2008. 8 A.D. Feb 27;

24. Curtis L NA. *Unit costs of Health and Social Care*. PSSRU, University of Kent, 2006.

11 Appendices

11.1. Draft search strategy

The draft Medline search strategy for the clinical effectiveness section of the review (reproduced below) will be adjusted as necessary for searching the other electronic databases listed in section 5.1.

Draft Medline Search strategy

1 exp obesity/ (44949)
2 Overweight/ (1562)
3 over?weight.ti,ab. (11311)
4 over weight.ti,ab. (106)
5 overeating.ti,ab. (440)
6 over?eating.ti,ab. (626)
7 exp Weight Loss/ (11322)

8 weight loss.ti,ab. (18540)
9 weight reduc$.ti,ab. (2722)
10 or/1-9 (66439)
11 bariatric surg$.ti,ab. (1788)
12 exp bariatric surgery/ (5414)
13 (surg$ adj5 bariatric).ti,ab. (1825)
14 anti?obesity surg$.ti,ab. (6)
15 antiobesity surg$.ti,ab. (6)
16 (obesity adj5 surgery).ti,ab. (842)
17 (obesity adj5 surgical).ti,ab. (503)
18 (gastroplasty or gastro?gastostomy or "gastric bypass" or "gastric surgery" or "restrictive surgery").ti,ab. (2723)
19 exp gastric bypass/ (2110)
20 exp jejunoileal bypass/ (159)
21 jejuno?ileal bypass.ti,ab. (75)
22 jejunoileal bypass.ti,ab. (75)
23 gastrointestinal surg$.ti,ab. (524)
24 gastrointestinal diversion$.ti,ab. (1)
25 exp biliopancreatic diversion/ (405)
26 biliopancreatic diversion.ti,ab. (304)
27 bilio?pancreatic diversion.ti,ab. (304)
28 biliopancreatic bypass.ti,ab. (14)
29 bilio?pancreatic bypass.ti,ab. (14)
30 gastric band$.ti,ab. (1033)
31 silicon band$.ti,ab. (5)
32 exp gastroenterostomy/ (2415)
33 gastrectomy.ti,ab. (4171)
34 gastrectomy.ti,ab. (4171)
35 gastroplasty/ (1745)
36 LAGB.ti,ab. (236)
37 stomach stapl$.ti,ab. (7)
38 lap band$.ti,ab. (165)
39 lap-band$.ti,ab. (165)
40 malabsorptive surg$.ti,ab. (7)
41 mason$ procedure.ti,ab. (9)
42 "Roux-en-Y".ti,ab. (1930)
43 anastomosis, Roux-en-Y/ (1338)
44 malabsorptive procedure$.ti,ab. (34)
45 duodenal switch$.ti,ab. (177)
46 stomach stapl$.ti,ab. (7)
47 obesity/su (746)
48 exp Obesity, Morbid/su [Surgery] (2991)
49 or/11-46 (12551)
50 10 and 49 (4612)
51 47 or 48 or 50 (4902)
52 limit 51 to yr="2001 - 2008" (4023)
53 limit 52 to humans (3963)
54 limit 53 to yr="2004 - 2008" (2914)
55 limit 54 to (clinical trial, phase iii or clinical trial, phase iv or clinical trial or comparative study or controlled clinical trial or evaluation studies or guideline or meta analysis or multicenter study or practice guideline or randomized controlled trial or "scientific integrity review" or technical report or twin study or validation studies) (555)
56 Cohort Studies/ (66145)
57 Randomized Controlled Trial/ (150030)
58 Prospective Studies/ (156648)

59 Evaluation Studies/ (96370)
60 Follow-Up Studies/ (185572)
61 (control$ or prospectiv$ or volunteer$ or placebo$ or random$).ti,ab. (1202900)
62 ((single$ or doubl$ or trebl$ or tripl$) adj (mask$ or blind$)).ti,ab. (47022)
63 or/56-62 (1477917)
64 54 and 63 (1130)
65 55 or 64 (1284)

11.2. Data extraction form

Surgery for morbid obesity – Draft Data extraction Form for Clinical Effectiveness Section of TAR Update 2008

Overwrite grey text with the details requested, use the abbreviations as listed below.

Characteristics of included study

Study	Methods	Participants	Interventions	Outcomes	Notes
first author year	DESIGN: e.g. single centre, RCT FOLLOW-UP: xx months.	COUNTRY: NUMBER: Total xx, GB xx, GP xx. AGE: SEX: BMI: WEIGHT: *Add others if reported* Characteristics of target population: Exclusion criteria:	1. name (abbreviation) details 2. name (abbreviation) details	*List primary and secondary outcome measures used : e.g.* Weight loss, Post operative mortality Morbidity rates, revision rates, Co-morbidities, QoL, Adverse effects *And point at which assessed if different from length of follow-up*	Method of data analysis: (ITT, point estimates given? confidence intervals given?) Sample size/power calculation:

Table of results

WEIGHT CHANGE	QOL / COMORBIDITY	EVENTS/PROCEDURES (COMPLICATIONS, REOPERATIONS)
OUTCOME:	OUTCOME:	OUTCOME:

Use these abbreviations:

ASGB = adjustable silicone gastric banding; AGB = adjustable gastric banding; BMI = body mass index; BPD = biliopancreatic diversion; GB = gastric bypass; Gband = gastric banding; GG = gastrogastrostomy; GIQLI = gastrointestinal quality of life index; GP = gastroplasty; Hand = hand-assisted laparoscopic Roux-en-Y gastric bypass; HRQL = Health Related Quality of Life; IBW = ideal body weight; ITT = intention to treat analysis; Lap = laparoscopic surgery; LASGB = laparoscopic adjustable silicone gastric banding; LGB = laparoscopic gastric bypass; LVGB = laparoscopic vertical banded gastroplasty; Open = open surgery; RCT = randomised controlled trial; RYGB = roux-en-Y gastric bypass; VBG = vertical banded gastroplasty; VLCD = very low calorie diet

Risk of bias

This table is based on the Risk of Bias Criteria set out in the draft of Chapter 8 for the new Cochrane Handbook (Handbook5_Bias_V9.pdf)

Item	Judgement	Description
Adequate sequence generation? (Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups)		
Allocation concealment? (Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, recruitment.)		
Blinding?* (Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.)		
Incomplete outcome data addressed?* (Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors)		
Free of selective outcome reporting? (State how the possibility of selective outcome reporting was examined by the review authors, and what was found.)		
Free of other sources of bias? (State any important concerns about bias not addressed in the other items in the tool. If particular questions/items were pre-specified in the review's protocol, responses should be provided for each question/item.)		

'Yes' indicates low risk of bias, 'No' indicates high risk of bias, 'Unclear' indicates uncertain risk of bias

** add a new row and give a Judgement and Description for each main outcome (or class of outcomes e.g. subjective and objective outcomes)*

(Delete if not required) **Quality criteria (CRD Report 4) for Observational studies**

Quality Item	Yes/No/Uncertain	Methodological Comments
Cohort studies		
1. Is there sufficient description of the groups and the distribution of prognostic factors?		
2. Are the groups assembled at a similar point in their disease progression?		
3. Is the intervention/treatment reliably ascertained?		
4. Were the groups comparable on all important confounding factors?		
5. Was there adequate adjustment for the effects of these confounding variables?		
6. Was outcome assessment blind to exposure status?		
7. Was follow-up long enough for the outcomes to occur?		
8. What proportion of the cohort was followed-up?		
9. Were drop-out rates and reasons for drop-out similar across intervention and unexposed groups?		