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HTA

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Abstract

The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation

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Objectives: To assess the clinical effectiveness and cost-effectiveness of bariatric surgery for obesity.

Data sources: Seventeen electronic databases were searched [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 databases; BIOSIS; and databases listing ongoing clinical trials] from inception to August 2008. Bibliographies of related papers were assessed and experts were contacted to identify additional published and unpublished references

Review methods: Two reviewers independently screened titles and abstracts for eligibility. Inclusion criteria were applied to the full text using a standard form. Interventions investigated were open and laparoscopic bariatric surgical procedures in widespread current use compared with one another and with non-surgical interventions. Population comprised adult patients with body mass index (BMI) ≥ 30 and young obese people. Main outcomes were at least one of the following after at least 12 months follow-up: measures of weight change; quality of life (QoL); perioperative and postoperative mortality and morbidity; change in obesity-related comorbidities; cost-effectiveness. Studies eligible for inclusion in the systematic review for comparisons of Surgery versus Surgery were RCTs. For comparisons of Surgery versus Non-surgical procedures eligible studies were RCTs, controlled clinical trials and prospective cohort studies (with a control cohort). Studies eligible for inclusion in the systematic review of cost-effectiveness were full cost-effectiveness analyses, cost-utility analyses, cost-benefit analyses and cost-consequence analyses. One reviewer performed data extraction, which was checked by two reviewers independently. Two reviewers independently applied quality assessment criteria and differences in opinion were resolved at each stage. Studies were synthesised through a narrative review with full tabulation of the results of all included studies. In the economic model the analysis was developed for three patient populations, those with BMI ≥ 40; BMI ≥ 30 and < 40 with Type 2 diabetes at baseline; and BMI ≥ 30 and <35. Models were applied with assumptions on costs and comorbidity.

Results: A total of 5386 references were identified of which 26 were included in the clinical effectiveness review: three randomised controlled trials (RCTs) and three cohort studies compared surgery with non-surgical interventions and 20 RCTs compared different surgical procedures. Bariatric surgery was a more effective intervention for weight loss than non-surgical options. In one large cohort study weight loss was still apparent 10 years after surgery, whereas patients receiving conventional treatment had gained weight. Some measures of QoL improved after surgery, but not others. After surgery statistically fewer people had metabolic syndrome and there was higher remission of Type 2 diabetes than in non-surgical groups. In one large cohort study the incidence of three out of six comorbidities assessed 10 years after surgery was significantly reduced compared with conventional therapy. Gastric bypass (GBP) was more effective for weight loss than vertical banded gastroplasty (VBG) and adjustable gastric banding (AGB). Laparoscopic isolated sleeve gastrectomy (LISG) was more effective than AGB in one study. GBP and banded GBP led to similar weight loss and results for GBP versus LISG and VBG versus AGB were equivocal. All comparisons of open versus laparoscopic surgeries found similar weight losses in each group. Comorbidities after surgery improved in all groups, but with no significant differences between different surgical interventions. Adverse event reporting varied; mortality ranged from none to 10%. Adverse

events from conventional therapy included intolerance to medication, acute cholecystitis and gastrointestinal problems. Major adverse events following surgery, some necessitating reoperation, included anastomosis leakage, pneumonia, pulmonary embolism, band slippage and band erosion. Bariatric surgery was cost-effective in comparison to non-surgical treatment in the reviewed published estimates of cost-effectiveness. However, these estimates are likely to be unreliable and not generalisable because of methodological shortcomings and the modelling assumptions made. Therefore a new economic model was developed. Surgical management was more costly than non-surgical management in each of the three patient populations analysed, but gave improved outcomes. For morbid obesity, incremental cost-effectiveness ratios (ICERs) (base case) ranged between £2000 and £4000 per QALY gained. They remained within the range regarded as cost-effective from an NHS decision-making perspective when assumptions for deterministic sensitivity analysis were changed. For BMI ≥ 30 and < 40, ICERs were £18,930 at two years and £1397 at 20 years, and for BMI ≥ 30 and <35, ICERs were £60,754 at two years and £12,763 at 20 years. Deterministic and probabilistic sensitivity analyses produced ICERs which were generally within the range considered cost-effective, particularly at the long twenty year time horizons, although for the BMI 30-35 group some ICERs were above the acceptable range.

Conclusions: Bariatric surgery appears to be a clinically effective and cost-effective intervention for moderately to severely obese people compared with non-surgical interventions. Uncertainties remain and further research is required to provide detailed data on patient QoL; impact of surgeon experience on outcome; late complications leading to reoperation; duration of comorbidity remission; resource use. Good-quality RCTs will provide evidence on bariatric surgery for young people and for adults with class I or class II obesity. New research must report on the resolution and/or development of comorbidities such as Type 2 diabetes and hypertension so that the potential benefits of early intervention can be assessed.

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*Due to the extensive nature of the appendices, these are available only in electronic format. The PDF file of the full report is available at www.ncchta.org/project/1742.asp. It will also be available on *HTA on CD* (see the inside front cover for full details).

List of abbreviations

AGB	adjustable gastric banding		HDU	high-dependency unit
AMI	acute myocardial infarction		HRQoL	health-related quality of life
BAROS	Bariatric Analysis and Reporting Outcome System		HSE	Health Survey for England
BMI	body mass index (kg/m²)		ICER(s)	incremental cost-effectiveness ratio(s)
BOSPA	British Obesity Surgery Patient Association		IGBP	isolated gastric bypass
BPD	biliopancreatic diversion		IHD	ischaemic heart disease
BSQ	Bing Scale Questionnaire		ITU	intensive-care unit
CEA	cost-effectiveness analysis		IQR	inter quartile range
CHD	coronary heart disease		ITT	intention to treat
CI	confidence interval		LAGB	laparoscopic adjustable gastric banding
CRD	NHS Centre for Reviews and Dissemination		Lap	laparoscopic surgery
CUA	cost–utility analysis		LDL	low-density lipoprotein
CVD	cardiovascular disease		LGBP	laparoscopic gastric bypass
DEALE	Declining Exponential Approximation to Life Expectancy		LISG	laparoscopic isolated sleeve gastrectomy
EMEA	European Medicines Agency		LOS	length of (hospital) stay
EQ-5D	European Quality Of Life-5 Dimensions		LRYGBP	laparoscopic Roux-en-Y gastric bypass
EWL	excess weight loss		LSG	laparoscopic sleeve gastrectomy
FHS	Framingham Heart Study		LVBG	laparoscopic vertical banded gastroplasty
GBand	gastric banding		LY(s)	Life year(s)
GBP	gastric bypass		MACL	Mood Adjective Check List
GERD	gastro-oesophageal reflux disease		MAQoL	Moorehead–Ardelt Quality of Life questionnaire
GIQLI	gastrointestinal quality of life index		NAO	National Audit Office
GP	general practitioner		NHANES	National Health and Nutrition Examination survey
HADS	Hospital Anxiety and Depression Scale		NICE	National Institute for Health and Clinical Excellence
HbA_{1c}	glycosylated haemoglobin		ns	not statistically significant
HCHS	Hospital and Community Health Services		Open	open surgery
HDL	high-density lipoprotein		PAssQ	Psychosocial Assessment Questionnaire

continued

PSS	personal social services	SHARE	Survey of Health, Ageing and Retirement in Europe
PCT(s)	primary-care trust(s)	SIGN	Scottish Intercollegiate Guidelines Network
PSSQ	Psychosocial Stress and Symptom Questionnaire	SOS	Swedish Obese Subjects
QALY(s)	quality adjusted life-year(s)	TC:HDL	total cholesterol to high-density lipoprotein ratio
QoL	quality of life	VAS	visual analogue scale
RCT(s)	randomised controlled trial(s)	VBG	vertical banded gastroplasty
RR	relative risk	VLCD(s)	very-low-calorie diet(s)
RYGBP	Roux-en-Y gastric bypass	vs	versus
SD	standard deviation	WHO	World Health Organization
SF-36	short form health survey		

Executive summary

Background

The prevalence of overweight and obesity among people in England and Wales is increasing. Associated serious health consequences in adults include Type 2 diabetes, cardiovascular disease, musculoskeletal disorders, certain cancers and increased mortality. Childhood obesity is associated with a higher chance of premature death and disability in adulthood. Obesity imposes a considerable economic burden on society. Weight loss improves obesity-related comorbidities and may have a mortality benefit. The intensity of intervention depends on the degree of obesity and presence of comorbidities. Management begins in primary care, but moves to the specialist setting when initial measures have failed and surgery is being considered. Bariatric (weight loss) surgery is increasing, but is not uniformly available across the country and a significant proportion is funded privately.

Objectives

To assess the clinical effectiveness and cost-effectiveness of bariatric surgery for obesity.

Methods

Data sources

Seventeen electronic resources, including MEDLINE, EMBASE and Cochrane, were searched from inception to August 2008. Bibliographies of related papers were assessed and experts were contacted to identify additional published and unpublished references.

Study selection

Titles and abstracts were screened for eligibility by two independent reviewers. Inclusion criteria were defined a priori and applied to the full text of retrieved papers by two independent reviewers using a standard form. The inclusion criteria were as follows:

- *Intervention* Open and laparoscopic bariatric surgical procedures in widespread current use.
- *Comparators* Surgical procedures in current use in comparison with one another; open surgery compared with laparoscopic surgery for the same procedure; surgical procedures in current use compared with non-surgical interventions (medical management, usual care or no treatment).
- *Population* Adult patients fulfilling the standard definition of obese [body mass index (BMI) of 30 or over] and young people who fulfil the definition of obesity for their age, sex and height.
- *Main outcomes* At least one of the following reported following a minimum of 12 months follow-up: measures of weight change; quality of life (QoL); perioperative and postoperative mortality and morbidity; change in obesity-related comorbidities; cost-effectiveness [reporting outcomes as either life-years or quality-adjusted life-years (QALYs)].

The study types that were eligible for inclusion were:

- *Systematic review of clinical effectiveness* Surgery versus surgery – randomised controlled trials (RCTs); surgery versus non-surgical procedure – RCTs, controlled clinical trials and prospective cohort studies (with a control cohort).
- *Systematic review of cost-effectiveness* Full cost-effectiveness analyses, cost–utility analyses, cost–benefit analyses and cost–consequence analyses.

Data extraction and quality assessment

Data extraction was undertaken by one reviewer and checked by two reviewers. Two reviewers independently applied quality assessment criteria. Differences in opinion were resolved through discussion at each stage.

Data synthesis

Studies were synthesised through a narrative review with full tabulation of the results of all included studies.

Economic model

The analysis was developed for three patient populations covered by studies included in the clinical effectiveness review:

- patients with morbid obesity BMI ≥40 undergoing adjustable gastric banding (AGB) or gastric bypass (GBP)
- patients with moderate-to-severe obesity (BMI ≥30 and <40) with significant comorbidity at baseline (Type 2 diabetes) undergoing AGB
- patients with moderate obesity (BMI ≥30 and <35) undergoing AGB.

A model developed previously was used for patients with morbid obesity (BMI ≥40), with updated assumptions on costs, diabetes incidence, permanency of diabetes remission following surgery, and on the impact of BMI on health-state utility.

A new model, including cardiac heart disease and stroke was applied in the analysis of AGB for moderate-to-severely obese (BMI ≥30 and <40) patients with Type 2 diabetes and for moderately obese (BMI ≥30 and <35) patients. The analysis was initially undertaken for the period of the trial follow-up only, but also included extrapolations up to 20 years following surgery.

Results

Quantity and quality of studies

A total of 5386 references were identified. Twenty-six studies (reported in 52 publications) were included in the review of clinical effectiveness. Three RCTs and three cohort studies compared surgery with non-surgical interventions; 20 RCTs compared different surgical procedures. Two studies focused on patients with a lower BMI (<35 or <40). The risk of bias of most of the trials was uncertain, only nine of the RCTs reported adequate sequence generation and only five reported adequate allocation concealment.

Summary of clinical effectiveness
Surgery versus non-surgical interventions

The evidence indicates that bariatric surgery is a more effective intervention for weight loss than non-surgical options. Surgery led to a greater reduction in weight in all six studies and the difference was statistically significant in five studies reporting a statistical comparison. In the two RCTs that reported outcomes at two years, mean per cent initial weight loss in the surgical groups was 20% and 21.6%, whereas the non-surgical groups had lost only 1.4% and 5.5% of their initial weight. In the two cohort studies reporting outcomes at two years, per cent weight change ranged from a weight loss of 16% to 28.6% in the surgical groups, but the non-surgical groups had gained weight with per cent weight change ranging from 0.1 to 0.5%. A large prospective cohort study [Swedish Obese Subjects (SOS) study] found that weight loss was still apparent 10 years following surgery, whereas patients receiving conventional treatment had gained weight. One RCT and one of two cohort studies assessing QoL found greater, and statistically significant, improvements after surgery on some measures, but not others. Two RCTs found that significantly fewer people had metabolic syndrome in the surgical group, and one found significantly higher remission of Type 2 diabetes following surgery. The SOS study found a statistically significant reduction in the incidence of three out of six comorbidities assessed at 10 years follow-up after surgery compared with conventional therapy.

Comparison of surgical procedures
Of the available surgical options assessed by RCTs there is evidence that GBP is more effective for weight loss than vertical banded gastroplasty (VBG) and AGB. Five of the seven included RCTs reported greater weight loss following GBP than VBG with per cent excess weight loss at one year ranging between 62.9% and 78.3% for GBP, and ranging between 43% and 62.9% for VBG. In two studies there was no statistically significant difference in 'success rate' or 'per cent ideal body weight'. One RCT found per cent excess weight loss of 66.6% was significantly greater up to five years following laparoscopic GBP than following laparoscopic AGB, which led to per cent excess weight loss of 47.5% ($p < 0.001$). Evidence from one RCT shows laparoscopic isolated sleeve gastrectomy to be more effective than AGB with greater excess weight loss up to three years (median per cent excess weight loss 66% versus 48%, $p = 0.0025$). GBP and banded GBP led to similar weight loss up to 24 months follow-up among patients with BMI > 50 (57.2% and 64.2%, $p = $ ns) in the single RCT making this comparison. Comparisons of GBP and laparoscopic sleeve gastrectomy (LSG), and of VBG and AGB produced equivocal results. One RCT found slightly greater per cent excess weight loss with LSG

(69.7%) than GBP (60.5%, $p = 0.05$) at 12 months, but no statistically significant difference in mean BMI or mean weight loss. Three RCTs found that measures of weight loss at one year follow-up favoured VBG over AGB, but longer-term results were conflicting. All the comparisons of open versus laparoscopic surgeries (GBP four RCTs; VBG one RCT; AGB one1 RCT) found that both groups lost similar amounts of weight.

QoL was assessed by only two RCTs. One RCT found that QoL was significantly better following GBP than VBG on some items. The other found that there was no significant difference in QoL following either open or laparoscopic GBP.

Changes in comorbidities after surgery were assessed by five of the 20 RCTs. In general, comorbidities improved in all groups with no significant differences in improvements observed between different surgical interventions.

Adverse events

The extent of reporting of adverse events varied between studies; few were compared statistically and none were powered to do so. Fourteen RCTs reported no deaths. Where deaths were reported separately for each RCT trial arm, mortality ranged from 2% (1/51 patients receiving Open GBP within the first 30 postoperative days) to 10% (2/20 patients receiving Open GBP, one on the fourth postoperative day, one after 13 months). The large SOS study reported mortality of 0.25% in the surgical cohort (5/2010 patients within 90 days of surgery). Adverse events from conventional therapy included intolerance to medication, acute cholecystitis and gastrointestinal problems. Major adverse events following surgery, some necessitating reoperation, included anastomosis leakage, pneumonia, pulmonary embolism, band slippage and band erosion.

Summary of cost-effectiveness

All modelled economic evaluations assessed in this report found that bariatric surgery was cost-effective in comparison to non-surgical treatment although the variability in estimates of costs and outcomes is large. The results of the economic evaluation alongside a clinical trial were inconclusive. However, because of the numerous methodological shortcomings and some poorly justified modelling assumptions the reported results are unlikely to be reliable and generalisable estimates of the incremental cost-effectiveness of bariatric surgery in comparison to non-surgical treatment.

Summary of economic model

Surgical management with GBP or AGB of morbid obesity (BMI > 40) was more costly than non-surgical management, but results in improved outcomes (in terms of QALYs) over the modelled 20-year time horizon. The incremental cost-effectiveness ratios (ICERs) ranged between £2000 and £4000 per QALY gained. The results were generally robust to changes in assumptions in the deterministic sensitivity analysis, and in all cases the ICERs remained within the range conventionally regarded as cost-effective from an NHS decision-making perspective.

Surgical management (with AGB) of moderate to severe obesity (BMI ≥ 30 and < 40) in patients with Type 2 diabetes was more costly than non-surgical management, but resulted in improved outcomes. The ICER reduced with a longer time horizon from £18,930 at two years to £1367 at 20 years. The results were generally robust to changes in assumptions in the deterministic sensitivity analysis. In the probabilistic sensitivity analysis the probability of surgical management being cost-effective (compared with non-surgical management) was 2.5% at a willingness-to-pay threshold of £20,000 per QALY and 50.6% at a willingness-to-pay threshold of £30,000 per QALY, for a two-year time horizon, and was 100% at both thresholds, for a 20-year time horizon.

Surgical management (with AGB) of moderate obesity (BMI ≥ 30 and < 35) was estimated to be more costly than non-surgical management, but resulted in improved outcomes, though the QALY gain at two years is small (0.08). The ICER reduced with a longer time horizon from £60,754 at two years to £12,763 at 20 years. There was considerable variability in results, in the deterministic sensitivity analysis, with ICERs above the range conventionally deemed acceptable in some scenarios even for longer time horizons. In the probabilistic sensitivity analysis the probability of surgical management being cost-effective (compared with an intensive medical programme) was 64% at a willingness-to-pay threshold of £20,000 per QALY and 98% at a willingness-to-pay threshold of £30,000 per QALY with a 20-year time horizon. In contrast, for a two-year time horizon, the probability of surgical management being cost-effective was zero at both thresholds.

Conclusions

Bariatric surgery appears to be a clinically effective and cost-effective intervention for moderately to severely obese people compared with non-surgical interventions. Uncertainties remain and further research is required, including:

- good-quality, long-term RCTs and cohort studies to provide detailed data on:
  – patient QoL to inform on the gains in utility associated with reduction in BMI
  – impact of surgeon experience on outcome of surgery
  – late complications leading to reoperation
  – more than one weight outcome measure with standard deviation about the mean reported to enable future meta-analysis
  – duration of remission of comorbidities and factors affecting this
  – resource use across the entire patient pathway to develop robust costings
- good-quality RCTs to provide evidence on bariatric surgery for young people and for adults with class I or class II obesity. New research must report on the resolution and/or development of comorbidities such as Type 2 diabetes and hypertension so that the potential benefits of early intervention can be assessed.
- A core set of important adverse bariatric surgery outcomes should be identified so that a standardised approach to describing adverse outcomes can be developed and their impacts on patients' QoL determined.

Chapter 1
Background

Description of health problem

Aetiology (cause of disease)

The development of obesity, at a simple level, occurs when energy taken into the body as food exceeds the amount of energy expended by the body. However, in reality, obesity is the outcome of a heterogeneous collection of disorders arising from a number of different causes. There is a complex interplay between genetic,[1] biochemical, neural and psychological factors, and external aspects such as environmental, social and economic factors.[2]

Natural history

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. However, the natural history of weight gain over time and progression to the development of overweight, obesity or morbid obesity have not been well documented. Some people are able to maintain a healthy weight throughout their life, but others will be at risk for weight gain. The age of onset and rate of progression of weight gain varies between individuals. Longitudinal studies have shown that age, sex and ethnicity are key risk factors for weight gain.[3–5] Such studies also suggest that, without intervention, reversal of overweight and obesity is uncommon.[4,6]

Classification (measurement of disease)

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 metres (kg/m^2). In adults overweight is most commonly defined as a BMI of 25 or over, obesity as a BMI of 30 or over, and severe or morbid obesity as a BMI of 40 or over (*Table 1*).[7,8] BMI (adjusted for age and gender) is also recommended by the National Institute for Health and Clinical Excellence (NICE) guideline on obesity[9] 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 recommends instead 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.

Epidemiology

Incidence

There is a large body of work reporting on the prevalence of obesity (see below), but much less information regarding the incidence of obesity. The published information regarding the incidence of obesity relates to the USA and Sweden, but no information has been found that is specific for the UK.

Adults

A recent study[10] evaluated trends in the incidence of overweight and obesity in the USA from 1950 to 2000 using data from the Framingham study participants. The results indicated that the overall incidence rates of overweight increased twofold, and that of obesity more than threefold over five decades. Per decade, there was an increase in the incidence of overweight of 25% in women and 20% in men. The corresponding per decade increases in women and men were 34% and 29% for the incidence of obesity, and 31% and 97% for the incidence of class II obesity.

A second study has compared trends in the incidence of overweight and obesity in a rural population from Sweden, and one from the USA between 1989 and 1999.[11] The 10-year incidence of overweight was similar in the two countries (337/1000 in Sweden, 336/1000 in the USA). However, the 10-year incidence of obesity was greater in the USA (173/1000) where 21.3% were obese in 1989 rising to 32.3% in 1999, than in Sweden (120/1000) where the prevalence of obesity was lower at both time points (9.6% in 1989 and 18.4% in 1999).

TABLE I *The international classification of adult underweight, overweight and obesity according to BMI[7,8]*

Classification	BMI	Risk of comorbidities
Underweight	< 18.5	Low (but risk of other clinical problems increased)
Normal range	18.50–24.99	Average
Overweight	≥ 25.00	
Preobese	*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)[a]	*≥ 40.00*	*Very severe*

BMI, body mass index.
a When BMI is over 50 this is sometimes referred to as 'super-obesity'.

Adolescents and children

Calculating the incidence of overweight or obesity in adolescents and children is particularly problematic. For adolescents who are approaching adulthood the difficulty lies in ensuring that the data sets employed in the study have used a definition of obesity that is comparable for the age groups of interest. Gordon-Larsen and colleagues[6] have used data from a longitudinal, nationally representative, school-based study of US adolescents and estimated that obesity incidence over the five-year study period was 12.7%. In contrast, fewer than 2% of the total sample of young adults who were obese as adolescents became non-obese.

The generalisability of the findings reported above to adults and children in the UK is unknown.

Prevalence
Adults

The World Health Organization (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.[12] 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).[13] In Wales in 2007, 57% of adults were classified as overweight or obese, including 21% obese.[14]

The prevalence of obesity (BMI > 30) among adults in England and Wales is increasing. In 2006 reported obesity prevalence in England was 23.7% for men and 24.2% for women. The increase was clear when the 2006 figures are compared with those for 1998 which were 17.3% for men

and 21.2% for women.[15] The 2006 prevalence of morbid obesity (BMI > 40)[16] was 2.1% (just under 863,000 people) with women being more likely to be morbidly obese than men (2.7% of women versus 1.5% of men). In comparison, the 1998 figures for morbid obesity were 0.6% for men and 1.9% for women. For a standard primary-care trust (PCT) population of 250,000, there would be 5250 cases of morbid obesity (based on the overall 2006 population value for England of 2.1% morbid obesity).

Prevalence of obesity increases with age, until age 55–64 years in men and until age 65–74 years in women, when it begins to decline[16] (*Table 2*). The number of men and women with obesity in England is shown in *Table 3*.[17,18] Obesity in women is more common in households where the current or former occupation of the household reference person is classified as routine and manual than in those households classified as intermediate, or managerial and professional (*Table 4*).[16] For morbid obesity in women the prevalence was 1.6% in managerial and professional households, but 4.0% in routine and manual households. Differences for men by category based on occupation was less marked.[16] Data from the Welsh Health Survey also indicate a rise in obesity among people aged 16 years and over from 18% in 2003–4 to 19% in 2005–6.[19]

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 using science-based methods. The Foresight project 'Tackling Obesities: Future Choices' produced a report made up of a number of

TABLE 2 *BMI among adults by age and gender 2006*[16]

	Age (years)							
	16–24 **%**	**25–34** **%**	**35–44** **%**	**45–54** **%**	**55–64** **%**	**65–74** **%**	**75 +** **%**	**Total** **%**
Men								
Underweight	5.5	0.2	0.4	0.1	0.5	0.4	0.6	1.2
Normal	60.8	37.7	26.5	23.7	19.9	19.2	30.5	31.7
Overweight	24.7	41.3	48.1	48.1	46.6	49.4	51.0	43.4
Obese	9.0	20.7	25.0	28.1	33.0	31.1	17.8	23.7
Overweight including obese	33.7	62.0	73.1	76.2	79.6	80.4	68.8	67.1
Morbidly obese	0.9	1.1	1.6	1.7	2.7	1.2	0.2	1.5
Mean BMI	*24.1*	*26.7*	*27.8*	*28.0*	*28.6*	*28.3*	*27.0*	*27.2*
Women								
Underweight	6.5	2.2	1.0	0.7	1.2	1.3	2.3	2.1
Normal	61.8	50.3	45.2	36.9	33.0	26.5	28.7	41.8
Overweight	19.7	29.2	30.1	35.2	35.7	37.5	41.6	31.9
Obese	12.0	18.2	23.7	27.2	30.2	34.7	27.4	24.2
Overweight including obese	31.7	47.5	53.8	62.4	65.9	72.2	69.0	56.1
Morbidly obese	1.4	2.0	3.1	3.1	3.4	3.6	1.6	2.7
Mean BMI	*24.0*	*25.9*	*26.8*	*27.6*	*28.0*	*28.6*	*27.5*	*26.8*

BMI, body mass index.

documents which 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.[20] Predicting trends in morbid obesity is more problematic. The Foresight modelling projection to 2050 suggests figures of 1% for males and 4% for females.[20] 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.[21]

TABLE 3 *Numbers with obesity by age and sex in England 2003*[17,18]

	Age (years)				
	16–34	**35–54**	**55–74**	**75 +**	**Total**
Men					
Overweight	2,066,211	3,281,310	2,349,520	706,323	8,403,365
Obese	851,769	1,848,110	1,305,710	296,998	4,302,588
Overweight including obese	2,917,981	5,129,420	3,655,231	1,003,321	12,705,953
Women					
Overweight	1,470,007	2,329,645	2,021,398	951,706	6,772,757
Obese	980,440	1,695,650	1,455,904	622,087	4,754,080
Overweight including obese	2,450,447	4,025,295	3,477,302	1,573,793	11,526,837

Numbers represent the estimated number of people within each age group who are either overweight, obese or overweight including obese.

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TABLE 4 *BMI by age and gender classified by occupation of the head of the household England 2003[16]*

	Men				Women			
	Occupation of head of household[a]				Occupation of head of household			
BMI	All adults (%)	Managerial and professional (%)	Intermediate (%)	Routine and manual (%)	All adults (%)	Managerial and professional (%)	Intermediate (%)	Routine and manual (%)
Underweight	1.4	1.3	0.6	1.9	2.1	2.1	1.3	2.3
Normal	33.2	32.1	33.0	34.6	42.3	48.1	43.0	36.2
Overweight	43.2	45.8	42.3	40.8	32.6	31.1	36.1	32.5
Obese	21.2	20.2	22.9	21.6	20.1	17.0	17.0	25.0
Morbidly obese	1.0	0.7	1.2	1.1	2.9	1.6	2.6	4.0
Overweight including obese	65.4	66.6	66.4	63.5	56.0	49.8	55.7	61.5

BMI, body mass index.
a Categories based on the current or last job of the household reference person. Where that person was a full-time student, had an inadequately described occupation, had never worked or was long-term unemployed they are included in the All adults column.

Children

As noted, overweight and obesity in children and young people are not defined according to a particular BMI. This means that varying prevalences of overweight and obesity in children and young people will be obtained depending on the particular definitions used.[22] This not only makes it difficult to obtain an accurate prevalence estimate, but also creates problems when trying to compare prevalences reported by studies employing different definitions. The NICE obesity guideline states that BMI measurement in children and young people should be related to the UK 1990 BMI charts to give age- and gender-specific information.[9]

Despite the difficulties in assessing the prevalence of overweight and obesity in children and young people there is general agreement that these are increasing. The National Statistics for England[16] report that between 1995 and 2005 the proportion of boys aged 2 to 15 years who were obese increased from 10.9% to 18.3%. For girls a similar pattern was seen with the proportion of obese 2–15-year-olds increasing from 12.0% in 1995 to 18.3% in 2005 (*Table 5*). In the 11–15 years age group the prevalence of obesity in 2005 was very similar in boys and girls at 20.4% and 20.8% respectively. In general the proportion of children who are obese increases with age until age 13–15 (*Table 6*).[16] These prevalence figures were derived using the UK

National BMI percentile classification to describe childhood overweight and obesity. This uses a BMI threshold for each age above which a child is considered overweight or obese. The classification estimates were produced by calculating the percentage of boys and girls who were over the 85th (overweight) or 95th (obese) BMI percentiles based on the 1990 UK reference population.

Impact of health problem

Obesity can have a variety of adverse health consequences including a risk of death. 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 progressively more overweight and obese.[12] The risks of obesity also apply to children as childhood obesity is associated with a higher chance of premature death and disability in adulthood.[12] The health consequences associated with obesity, such as those listed in *Table 7*, impose a considerable economic burden on society.

Health risks of overweight and obesity
The current NICE guideline on obesity[9] recommends that the assessment of the health risks associated with overweight and obesity in adults should be based on BMI and waist circumference (*Table 8*). The proportion of English men and women who fall into different health risk categories

TABLE 5 *Overweight and obesity prevalence among children in England by age and gender for 1995 and 2005*[16]

	Overweight		Obese		Overweight including obese	
	1995	2005[a]	1995	2005[a]	1995	2005[a]
Boys						
Aged 2–10	12.9	16.1	9.6	16.9	22.5	33.0
Aged 11–15	13.4	15.0	13.5	20.4	26.9	35.3
Aged 2–15	13.1	15.7	10.9	18.3	24.0	33.9
Girls						
Aged 2–10	12.6	12.2	10.3	16.8	22.9	29.0
Aged 11–15	13.9	14.1	15.4	20.8	29.3	34.9
Aged 2–15	13.1	12.9	12.0	18.3	25.0	31.2

a   From 2003 data were weighted for non-response.

as defined in the NICE guidelines have been estimated by the National Statistics Information Centre (*Table 9*).[16]

Health consequences of overweight and obesity

The COUNTERWEIGHT program, which has been developed and evaluated to be an effective model for obesity management with general practice in the UK, undertook a cross-sectional survey of the records of 6150 obese adults. It found that obese patients made significantly more visits to their general practitioner (GP), practice nurse and hospital outpatient departments than patients classified as normal weight, even after adjustments had been made for confounding factors.[23] Over the last 10 years there were 17,458 Finished Consultant Episodes with a primary diagnosis of obesity. Almost a quarter of these (4068) occurred in 2006–7.[16]

Health consequences in adults

The predominant serious health consequences associated with overweight and obesity in adults include Type 2 diabetes, cardiovascular disease (CVD) (mainly heart disease and stroke), musculoskeletal disorders such as osteoarthritis, and certain cancers (*Table 7*) and are discussed in more detail below. As indicated in *Table 8* and *Table 9* the risk of serious health consequences increases with increasing obesity (greater detail is provided in Chapter 5, Data sources, Effectiveness data). Some of these health consequences may constitute the principal cause of death, e.g. heart disease, stroke, some cancers; whereas, others such as Type 2 diabetes lead to a reduced life expectancy. Other important health consequences that have a negative impact on quality of life (QoL) are obstructive sleep apnoea, infertility, obstetric complications and psychiatric comorbidity.

TABLE 6 *Obesity prevalence by age*[16]

	2002–2004[a]	
Age (years)	Obese %	Overweight including obese %
2–3	11.6	25.2
4–5	12.8	27.2
6–7	13.5	26.7
8–10	18.7	31.8
11–12	22.0	37.6
13–15	19.5	34.1

a   Data aggregated over three years to achieve a sufficiently large sample for analysis at this level.

TABLE 7 *Estimated increased risk for the obese of developing obesity-associated diseases*

Disease	Relative risk[a] – women (England)[24]	Relative risk[a] – men (England)[24]	WHO estimate of increased risk (men and women worldwide)[8]
Type 2 diabetes	12.7	5.2	Greatly increased
Dyslipidaemia	–	–	Greatly increased
Insulin resistance	–	–	Greatly increased
Breathlessness	–	–	Greatly increased
Sleep apnoea	–	–	Greatly increased
Cardiovascular disease	–	–	Moderately increased
Myocardial infarction	3.2	1.5	
Angina	1.8	1.8	
Stroke	1.3	1.3	
Hypertension	4.2	2.6	Moderately increased
Cancer of the colon	2.7	3.0	Slightly increased
Gall bladder diseases	1.8	1.8	Greatly increased
Osteoarthritis	1.4	1.9	Moderately increased (knees)
Hyperuricaemia and gout	–	–	Moderately increased
Ovarian cancer	1.7	–	
Breast cancer in postmenopausal women	–	–	Slightly increased
Endometrial cancer	–	–	Slightly increased
Reproductive hormone abnormalities	–	–	Slightly increased
Polycystic ovary syndrome	–	–	Slightly increased
Impaired fertility	–	–	Slightly increased
Fetal defects associated with maternal obesity	–	–	Slightly increased
Low back pain due to obesity	–	–	Slightly increased
Risk of anaesthesia complications	–	–	Slightly increased

WHO, World Health Organization.
a   All relative-risk values are approximate.

The WHO finds that the relative risks of particular disease in obese people, compared with lean people, are fairly similar throughout the world and have classified these into three broad categories: greatly increased risk (relative risk much greater than 3); moderately increased risk (relative risk 2–3); and slightly increased risk (relative risk 1–2) (*Table* 7).[8] The best estimates of the increased disease risk due to obesity for the English population were calculated from international studies by the National Audit Office[24] for a number of these conditions and these risk estimates are also shown alongside the WHO estimates in *Table* 7. Although the results should be interpreted with some caution (some studies that contributed data used an alternative cut-off point for obesity instead of the widely used definition of a BMI of 30 or above) they do provide a broad indication of the strength of the association between obesity and disease.

Increased mortality
Obesity significantly increases the risk of mortality at any given age (including after adjustment for other risk factors such as smoking) and those who have been overweight for the longest are at the highest risk. The National Audit Office (NAO) has reported that evidence from studies suggests that young adults with a BMI of 30 have a mortality risk that is about 50% higher than that of a young adult with a healthy BMI (18.5–25).[24] For a young adult with a BMI of 35 the mortality risk is more than doubled. One study reported that 40-year-old obese (BMI greater than or equal to 30) women

TABLE 8 *NICE guideline recommendation for the assessment of health risks associated with overweight and obesity[9]*

Waist circumference	BMI classification	
	Overweight	Obesity I[a]
Low Men < 94 cm; Women < 80 cm	No increased risk	Increased risk
High Men 94–102 cm; Women 80–88 cm	Increased risk	High risk
Very high Men > 102 cm; Women > 88 cm	High risk	Very high risk
BMI, body mass index a As defined in *Table 1*.		

and men lost 7.1 and 5.8 years of life, respectively, compared with 40-year-old non-smoking women and men of normal weight.[25] In 2004, a House of Commons Select Committee report estimated that 6.8% of all deaths in England were attributable to obesity.[26]

Type 2 diabetes

Type 2 diabetes is the most common form of diabetes, accounting for over 90% of all diabetes in the UK.[13] It is characterised by insulin resistance and is a serious life-shortening condition. The 'first-line' treatment is diet, weight control and physical activity but drug therapy, e.g. with metformin, sulphonylurea drugs, thiazolidinediones (commonly called glitazones), or insulin therapy may become necessary. The risk of developing diabetes rises with increasing BMI even below the threshold of clinical obesity. The Health Survey for England (HSE) data have been used to examine the association between a number of risk factors and Type 2 diabetes in adults aged 35 years and over. Men and women who were obese had approximately double the odds of having Type 2 diabetes compared with those who had a BMI of less than 25 (after adjusting for other factors). A raised waist circumference was also linked to increased odds of having Type 2 diabetes, in men the odds were doubled, whereas women with a raised waist circumference were four times more likely to have Type 2 diabetes than those without a raised waist circumference measurement.[13]

Cardiovascular disease and CVD risk factors

The term CVD encompasses ischaemic heart disease (IHD) [also known as coronary heart disease (CHD)], stroke and peripheral vascular disease. Obesity is an independent risk factor for CVD. Data from the HSE 2003[17] demonstrate that a relationship between IHD and BMI is present in men and women. The prevalence of

TABLE 9 *Percentage of adults within each health-risk category associated with overweight and obesity in adults by gender 2006[16]*

	Men					Women				
	Over-weight	Obesity I	Obesity II	Obesity III	All	Over-weight	Obesity I	Obesity II	Obesity III	All
No increased risk	13				45	4				45
Increased risk	19	0			20	12	0			14
High risk	11	3			13	15	1			16
Very high risk		15	4	1	21		14	6	3	23
Grey shading indicates that health-risk category does not apply at this level of overweight or obesity, e.g. people who are overweight and have a very high waist circumference measurement do not fall into the very high health-risk category (as shown in *Table 8*), and those with the lowest waist circumference measurement and class I obesity have an increased health risk (therefore the 'No increased health risk' category is not applicable).										

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IHD or stroke was lowest among people with a normal BMI, but increased for people in the overweight category and was highest among obese women and men. However, in women, the higher prevalence in the obese was no longer significant following age standardisation (*Table 10*). A raised waist circumference is also linked to an increased prevalence of CVD in men and women.

Hypertension is a key risk factor for CVD and the positive association between blood pressure and BMI is well documented. Data from the HSE 2003[17] shows that overweight men and women (BMI between 25 to less than 30) and obese men and women (BMI 30 or more) both have a higher blood pressure than those with a normal BMI (*Table 11*). The link between high blood pressure and obesity was also observed during the HSE 2005 which focused on people aged 65 years and over.[27] In this age group hypertension was twice as common in obese men and women, and more prevalent in overweight women, compared with those with a weight in the normal range.

Abnormalities in serum lipid levels [raised total cholesterol, triglycerides and low-density lipoprotein (LDL), with reduced high-density lipoprotein (HDL)] are a further risk factor for CVD. The National Health and Nutrition Examination Survey (NHANES) III[28] found that the prevalence of raised cholesterol (≥ 240 mg/dl) in obese men and women was 22% and 27%, respectively, compared with 13% of adults with BMI < 25. HDL-cholesterol decreased with increasing BMI. The prevalence of low HDL-cholesterol (< 35 mg/dl men, < 45 mg/dl women) in obese adults was 31% of men and 41% of women compared with 9% and 17%, respectively, in adults with desirable weight. A more recent publication employing data from the survey of health, ageing and retirement in Europe (SHARE) also found that the odds ratios for high cholesterol were significantly increased for overweight and obese adults.[29]

Cancer
A systematic review and meta-analysis of prospective observational studies reported that in men, a 5 kg/m² increase in BMI was strongly associated with oesophageal adenocarcinoma [relative risk (RR) 1·52, $p < 0·0001$] as well as thyroid (1·33, $p = 0·02$), colon (1·24, $p < 0·0001$) and renal (1·24, $p < 0·0001$) cancers. For women, the strong associations were between a 5 kg/m² increase in BMI and endometrial (1·59, $p < 0·0001$), gall bladder (1·59, $p = 0.04$), oesophageal adenocarcinoma (1·51, $p < 0·0001$) and renal (1·34, $p < 0·0001$) cancers. There were also weaker positive associations between increased BMI and some other cancers in both men and women.[30] As health risks increase with increasing obesity, increases in BMI greater than 5 kg/m² may be associated with greater cancer risks.

A study assessing the cost of obesity to the UK estimated that the cancers with some relationship with overweight and obesity (breast cancer, colon/rectum cancer and corpus uteri cancer) were responsible for 6.2% of all mortality.[31]

TABLE 10 *Relationship between BMI and ischaemic disease*[17]

	Observed prevalence 2003		Age-standardised prevalence 2003	
	Any CVD (%)	**IHD or stroke**	**Any CVD (%)**	**IHD or stroke**
Men				
Normal range	10	4	10	5
Overweight	14	8	11	6
Obese	17	10	13	8
Women				
Normal range	10	3	11	4
Overweight	13	6	12	5
Obese	16	7	14	6

BMI, body mass index; CVD, cardiovascular disease; IHD, ischaemic heart disease.
Normal range = BMI over 18.5–25, overweight = BMI over 25–30, obese = BMI over 30

TABLE 11 *Relationship between overweight or obesity and blood pressure in men and women[17]*

	Difference from the reference category mmHg (95% CI)
Men	
Reference category: normal range	0
Overweight	2.86 (1.15 to 4.21)
Obese	6.22 (4.71 to 7.73)
Women	
Reference category: normal range	0
Overweight	3.32 (2.29 to 4.34)
Obese	6.02 (4.76 to 7.29)

BMI, body mass index; CI, confidence interval.
Normal range = BMI over 18.5 to 25, overweight = BMI over 25 to 30, obese = BMI over 30.

Osteoarthritis

Osteoarthritis, or degenerative disease of the knee and other weight-bearing joints, and lower back pain are common in obesity. Some effects are thought to be the result of excess weight; BMI has been associated with the incidence and progression of knee osteoarthritis, but not associated with the incidence and progression of hip osteoarthritis. However, it has also been postulated that some obesity-related osteoarthritis may be the result of a metabolic effect.[32,33] Whatever the cause, an estimated 27% of hip replacements and 69% of knee replacements in middle-aged women in the UK are attributable to obesity.[34]

Respiratory disorders

Respiratory disorders such as obstructive sleep apnoea are associated with obesity. It has been estimated that approximately 17% of adults aged 30–69 years in the USA have sleep-disordered breathing graded as 'mild or worse' and it is further estimated that in 41% of these adults their sleep-disordered breathing can be attributed to having a BMI ≥25. The study has similarly estimated that 5.7% of adults have sleep-disordered breathing graded 'moderate or worse' which in 58% of cases may be attributed to excess weight.[35]

Reproductive disorders

Reproductive disorders are common in obesity, occurring in both women and men. Cohort studies have identified obese women as having a higher risk of complications during pregnancy, such as pregnancy-induced hypertension, antepartum venous thromboembolism, induction of labour, caesarean delivery and wound infection, pre-eclampsia, premature labour, gestational diabetes and macrosomia (large-for-date fetuses).[36–40] Some studies have found evidence for an increased risk of adverse pregnancy outcomes such as perinatal death,[41] but others have not found evidence for an increased risk.[38]

Health consequences in children and young people

Overweight and obese children and young people are at high risk of developing comorbidities, either while still young, or as they progress into adulthood. The current NICE Obesity guideline recommends that assessment of comorbidity should be considered for children with a BMI at or above the 98th centile.

It is not surprising that studies reporting on the health consequences of overweight and obesity in children and young people have found many of the comorbid conditions described above for adults.[42–45] However, caution should be exercised in applying findings from one population to another. One recent study aimed to investigate the prevalence of comorbidity in a population representative of the general obese childhood population in the UK and found that the prevalence of abnormal blood test results (e.g. for insulin, glucose, triglycerides and cholesterol) may be lower than those published in the USA and from a UK tertiary referral centre (Great Ormond Street, London, UK).[46]

Other health consequences

There are likely to be a number of other potential health consequences that have not been mentioned above which are associated with overweight and obesity but for which, at the moment, there are insufficient data to enable the health risks to be

robustly estimated. For example, there is emerging evidence that suggests obese people are more likely than people of normal weight to develop various types of infection, including postoperative infections.[47]

Benefits of weight loss

Although the success of weight loss interventions are often expressed in terms of the amount of weight lost, improvements in QoL and comorbidities are generally a more meaningful indication of success for individuals.[48–50] A systematic review of the long-term effects of obesity treatments on body weight, risk factors for disease and disease[51] 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 LDL-cholesterol, total cholesterol and blood pressure, in the long term. The effects of bariatric (weight loss) surgery on weight and Type 2 diabetes have also been reviewed.[52] The authors reported that bariatric surgery not only led to weight reduction, but also that preoperative diabetes resolved postsurgery in more than 75% of cases. A further systematic review of the long-term weight loss effects on all-cause mortality in overweight/obese populations[53] 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. Weight loss in obese patients with knee osteoarthritis has also been systematically reviewed and the results of meta-analysis indicated that disability could be significantly improved when weight was reduced over 5.1%, or at the rate of $> 0.24\%$ reduction per week.[54] Weight loss has not been found to have a beneficial effect on risk of stroke.[55]

Adverse effects of weight loss

It is important that obese patients are made aware of the potential adverse effects of weight loss so that they can come to a judgement about the balance between the risks and benefits of the approaches to weight loss that they are considering.[49,50,56] Not only are adverse effects associated with the various pharmaceutical and surgical interventions for achieving weight loss, but adverse effects are also associated with dietary regimens. In particular rapid weight loss is an important risk factor for gallstone development, there is evidence that obese women who lose 4–10 kg in weight have a 44% increase in risk of gallstones caused by the increase in circulating cholesterol.[8] However, it has been estimated that

the incidence of gallstone formation is unchanged below rates of weight loss of 1.5 kg per week.[57] Weight loss may also decrease bone density.[8] Contradictory evidence has been published with regard to the effect of weight loss and mortality. A recent review of the evidence has suggested that the impact of weight loss may be gender specific, there was some evidence for long-term benefits on mortality in women, but the long-term effects for men were not clear.[53]

Current service provision

Management of disease

Non-surgical interventions are the cornerstone of overweight and obesity treatment. The 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.

Adults

Management initially takes place within the general practice setting provided by the GP or practice nurse. As the degree of overweight increases, and depending on the presence or absence of comorbidities, intensity of management should increase to include dietary, physical exercise and lifestyle advice. The current NICE obesity guideline[9] states that multicomponent interventions are the treatment of choice. Weight management programmes should include behaviour change strategies to increase people's physical activity levels or decrease inactivity, improve eating behaviour and the quality of the person's diet and reduce energy intake.[9] The NICE guideline suggests that in adults a prescription for drugs for weight control should be considered for people who are overweight with obesity-related comorbidities (BMI 25.00–29.99) or who meet the criteria for class I obesity (BMI 30.00–34.99) with obesity-related comorbidities, or who meet the criteria for class II obesity (BMI 35.00–39.99). The currently approved drugs are orlistat, sibutramine and, for obese people who have tried orlistat and sibutramine or who are unable to tolerate these two drugs, rimonabant. The NICE obesity guideline lists the situations when onward referral to specialist care should be considered:

- the underlying causes of overweight and obesity need to be assessed
- the person has complex disease states and/or needs that cannot be managed adequately in either primary or secondary care

- conventional treatment has failed in primary or secondary care
- drug therapy is being considered for a person with a BMI more than 50
- specialist interventions [such as a very-low-calorie diet (VLCD) for extended periods] may be needed
- surgery is being considered.

Surgery is usually considered a last resort intervention. NICE obesity guidelines recommend bariatric surgery as a treatment option only when all of the listed criteria are fulfilled:

- the person has a BMI of 40 or more, or a BMI between 35 and 40 and other significant disease (for example, Type 2 diabetes or high blood pressure) that could be improved with weight loss
- all appropriate non-surgical measures have been tried but have failed to achieve or maintain adequate, clinically beneficial weight loss for at least six 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.

The guidelines also recommend bariatric surgery as a first-line option (instead of lifestyle interventions or drug treatment) for adults with a BMI of more than 50 in whom surgical intervention is considered appropriate.

Children and young people

As with adults, management initially takes place within the general practice setting provided by the GP or practice nurse. The NICE Obesity guideline[9] indicates that BMI measurement in children and young people should be related to the UK 1990 BMI charts to give age- and gender-specific information. A tailored clinical intervention should be considered for children with a BMI at or above the 91st centile, depending on the needs of the individual child and family. NICE guidelines do not recommend a dietary approach alone for children and young people. Instead any dietary recommendations must be part of a multicomponent intervention. For children with a BMI at or above the 98th centile an assessment of comorbidity should be considered.

Referral to an appropriate specialist should be considered for children who are overweight or obese and have significant comorbidity or complex needs (for example, learning or educational difficulties). In secondary care, the assessment of overweight or obese children and young people should include assessment of associated comorbidities and possible aetiology. This can include investigations of blood pressure, fasting lipid profile, fasting insulin and glucose levels and liver and endocrine functions.

Orlistat and sibutramine do not have UK marketing authorisation for use in children; however, the NICE obesity guideline does not preclude their use in children. In children younger than 12 years, drug treatment may be used only in exceptional circumstances, e.g. if severe life-threatening comorbidities are present, and only in specialist paediatric settings. In children aged 12 years and older, treatment with orlistat or sibutramine may be started in a specialist paediatric setting by multidisciplinary teams experienced in prescribing for this age group. However, treatment is only recommended if physical comorbidities or severe psychological comorbidities are present. Rimonabant has recently been approved by NICE for use in adults when certain conditions are met, but it is not approved for use in children.

NICE obesity guidelines do not recommend bariatric surgery as a general treatment option for obese children and young people. However, the guideline acknowledges that there may be exceptional circumstances in which bariatric surgery can be considered providing the young person has achieved, or nearly achieved physiological maturity.

Current service cost

A recent study has estimated the direct cost of overweight and obesity to the NHS at £3.2 billion.[31] The majority of the costs attributable to overweight and obesity were the result of stroke, CHD, hypertensive disease and diabetes mellitus. This study was based on including people with a BMI of 22 and above, and because cost estimates are very sensitive to the BMI cut-off point chosen, the cost estimate from this study is higher than those of other studies.

A House of Commons Health Committee report[26] estimated the direct treatment costs of obesity for 2002 were between £46 million and £49 million. The costs included in calculating this estimate were those for GP consultations, ordinary admissions, day cases, outpatient attendances and

prescriptions. The cost estimate for treating the consequences of obesity (comorbidities) in 2002 was between £945 million and £1075 million. When the direct treatment costs and consequences of obesity costs were combined the total range for the direct costs of treating obesity and its consequences for 2002 was £990 to 1225 million (2.3–2.6% of net NHS expenditure in 2001–2). These figures were based on including people with a BMI of 25 and over, this is one reason why the estimate may be lower than for the more recent study above. However, it must be acknowledged that the Health Committee report stresses that these figures are still likely to underestimate the true cost of treating obesity and its consequences.

Relevant national guidelines

Three pieces of guidance with relevance to the UK are:

- Obesity: the prevention, identification, assessment and management of overweight and obesity in adults and children. NICE clinical guideline 43. Issue date: December 2006.[9] This guideline replaces three earlier pieces of NICE guidance [TA22 Obesity–orlistat, TA31 Obesity–sibutramine and TA46 Obesity (morbid)–surgery] and largely supersedes the 2003 Royal College of Physicians report 'Anti-obesity drugs. Guidance on appropriate prescribing and management'.[58]
- Rimonabant for the treatment of overweight and obese patients. NICE Technology appraisal. Issue date June 2008.[59] NICE has temporarily withdrawn its guidance on the use of rimonabant for the treatment of overweight and obese patients. The withdrawal of this guidance follows the decision of the European Medicines Agency (EMEA) in October 2008 to recommend suspension of the marketing authorisation for rimonabant. The EMEA concluded that the benefits of rimonabant no longer outweigh its risks. NICE will continue to review the status of its guidance in light of any further changes to rimonabant's marketing authorisation.
- The Scottish Intercollegiate Guidelines Network (SIGN) is in the process of updating it guidance on obesity.

Description of technologies under assessment

Surgical procedures for those with obesity aim to reduce weight and maintain any loss through restriction of intake and/or malabsorption of food. It is hoped that as a consequence eating behaviour is modified, with patients consuming smaller quantities of food more slowly. In addition to modifying eating habits, patients are encouraged to commit to daily exercise as part of a wider change in lifestyle. Surgery for obesity is a major surgical intervention with a risk of significant early and late morbidity and of perioperative mortality. Contraindications for bariatric surgery include poor myocardial reserve, significant chronic obstructive airways disease or respiratory dysfunction, non-compliance of medical treatment and psychological disorders of a significant degree.

Before surgery, patients should be made aware of the nature of the procedure and how it fits into the overall management programme for morbid obesity. Particularly important before surgery are the preoperative breathing exercises to reduce the incidence and severity of postoperative pulmonary insufficiency and assessment through spirometry. Patients may require antibiotic prophylaxis at anaesthesia and prophylactic measures to guard against perioperative thromboembolic disease. It is rare that patients will require ventilatory support and many, particularly if the surgery has been conducted laparoscopically, will not require intensive care nursing in a high dependency unit.

Several different surgical procedures have been used for people with morbid obesity. This review will focus on the principal types of surgical procedure that are in current use, including gastric bypass, gastric banding, biliopancreatic diversion and vertical banded gastroplasty. Of the procedures in current use gastric bypass and gastric banding are much more commonly performed than the others. Procedures that are no longer practised, such as jejunoileal bypass and horizontal gastroplasty, are not considered by this report. The following section briefly discusses these procedures and their complications. The section does not provide a comprehensive discussion of the many variants of these procedures that have developed. Intragastric balloons are not discussed because these are considered a short-term or temporary measure and not a comparator for the other surgical procedures.

Gastric bypass

The Roux-en-Y and resectional gastric bypass procedures combine restriction and malabsorption techniques, creating both a small gastric pouch and a bypass that prevents the patient from absorbing all they have eaten.[15] The Roux-en-Y procedure

entails partition of the upper part of the stomach using surgical staples to create a small pouch (50 ml or less) with a small outlet (gastroenterostomy stoma) to the intestine that is attached to the pouch. The Roux-en-Y technique is used to avoid loop gastroenterostomy and the bile reflux that may ensue. Adaptations of the procedure include lengthening of the Roux-en-Y limb to 100–150 cm and use of retrocolic and retrogastric routing of the gastrojejunostomy. Often a prosthetic band, such as a Silastic ring or Gortex band, is positioned above the junction of the gastric pouch and small intestine to stabilise the gastroenterostomy, preventing late stretching of the opening and improving long-term weight control. Banded gastric bypass is not undertaken in the UK and because there is some disagreement as to whether it constitutes a separate procedure it is considered separately in this review. It is technically possible to reverse a gastric bypass. All patients who undergo gastric bypass procedures need long-term vitamin B_{12} replacement and oral iron therapy. Patients may be at risk from postgastrectomy bone disease. Advice on diet suggests a liquid diet for several weeks after the operation and improved eating habits involving small meals and multivitamin supplementation. Typically gastric bypasses which are performed laparoscopically require up to three to five days of inpatient stay (the open procedure, which is rarely undertaken now, requires a longer inpatient stay), with most patients unable to go back to work until after one month following surgery.

Complications associated with gastric bypass include failure of the staple partition, leaks at the junction of the stomach and small intestine, acute gastric dilatation, delayed gastric emptying either spontaneously or secondary to a blockage of the efferent limb. Failures of the staple line have been overcome by either transection of the stomach (staple line is divided and the cut ends over sewn) or superimposed staple rows causing firm scarring along the staple line. Other complications may occur following surgery including: vomiting caused by narrowing of the stoma as the result of scar tissue development, correctable through stretching by use of an endoscopic balloon dilatation as a day case; wound hernias and intestinal obstruction; anaemia as a result of lack absorption of iron and vitamin B_{12} 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). It is thought that the dumping syndrome aids weight loss by conditioning the patient against eating sweets.

Adjustable 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. Adjustment is undertaken without the need for surgery by adding or removing saline through a subcutaneous access port. As a restrictive procedure, gastric banding avoids the problems associated with malabsorptive techniques. Gastric banding is technically a reversible procedure. Surgery to fit an adjustable gastric band is typically undertaken laparoscopically and involves a short hospital stay, usually a maximum of two or three days. Following surgery, patients are usually seen regularly until they achieve their target weight and then on an infrequent basis thereafter. Often patients will be advised on nutrition postoperatively.

Complications include those associated with the operative procedure, 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,[60] with major reoperations required by over 20% of patients after mean follow-up periods of about five years.[61,62] Expert opinion suggests that band failure rate may be greater than this, possibly approaching 30%.

Biliopancreatic diversion

Biliopancreatic diversion was first reported in 1978 by Scopinaro.[63] It has become popular in Europe and is primarily a malabsorptive procedure. The standard procedure involves the removal of part of the stomach (a limited horizontal gastrectomy) to limit oral intake and induce weight loss. The gastric pouch which is created is larger than that of gastric bypass or the restrictive procedures therefore allowing larger meals, and patients remain on a less restricted diet than would be the case following gastric bypass. Part of the small intestine is also bypassed (the malabsorptive component) by the

construction of a long limb Roux-en-Y anastomosis with a short common 'alimentary' channel of 50 cm length. As the procedure does not defunctionalise any part of the small intestine fewer liver problems are caused than occurred with jejunoileal bypass procedures.[64] Biliopancreatic diversion is only a partially reversible procedure. The combination of biliopancreatic diversion with duodenal switch is an additional adaptation of the standard procedure. It has a sleeve gastrectomy rather than a horizontal gastrectomy. Length of hospital stay for biliopancreatic diversion ranges between two and seven days.

Biliopancreatic diversion is considered to be a technically demanding procedure with an operative mortality of 2% and major perioperative morbidity of 10%.[65] Side effects of the procedure include loose stools, stomal ulcers, offensive body odour and foul smelling stools and flatus. Serious complications include anastomotic leak and anastomotic ulceration (3%–10%), protein malnutrition (3%–4%), hypoalbuminaemia, anaemia (< 5%), oedema, asthenia (lack of energy) and alopecia (hair loss).[65,66] In some instances patients require further hospitalisation and hyperalimentation. As a result of malabsorption, patients usually need calcium and vitamin supplements and lifelong follow-up. In an attempt to overcome these complications, particularly stomal ulceration and diarrhoea, several variants of the procedure have been developed. Sleeve resection of the stomach maintains continuity of the gastric lesser curve while the duodenal switch maintains continuity of the gastroduodeno–jejunal axis.

Sleeve gastrectomy

For some patients who are at high risk from bariatric surgery a sleeve gastrectomy is considered. This is generally seen as the first part of a two-part surgical procedure, being followed at a later date by a conversion to either a gastric bypass or a duodenal switch. However, for some, enough weight is lost with the sleeve gastrectomy alone. The sleeve gastrectomy divides the stomach vertically to reduce its size to about 25%. It leaves the pyloric valve at the bottom of the stomach intact, which means that the stomach function remains unaltered and digestion is therefore unaltered. After 6–12 months the stomach may have expanded and does not restrict intake as much, this is when the gastric bypass can then be added if necessary. The sleeve gastrectomy is not reversible.

Complications are reduced because digestion is unaffected; however, patients are at risk from leaking from the newly formed stomach or vomiting as a result of over-eating. As with all surgery, there is a risk from postoperative complications such as postoperative bleeding and small bowel obstruction.

This operation is relatively quick to perform, which reduces the risk from complications. Hospital stay is normally one or two days.

Vertical banded gastroplasty

Vertical banded gastroplasty is now used infrequently; however, it has been used in a number of studies as the comparator intervention and hence is included here. Vertical banded gastroplasty partitions the stomach, 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. In addition, a polypropylene band may be used around the lower end of the vertical pouch to prevent stretching. 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. The only restrictions are that people should chew food thoroughly to avoid vomiting and high-calorie liquids should be avoided. Vertical banded gastroplasty usually requires similar inpatient stay and time to return to work as gastric bypass, up to 10 days hospitalisation and return to work after at least a month.

Complications are relatively rare, with a low postoperative mortality rate (1%). Revision rates requiring further surgical intervention are often high at approximately 30%. Specific complications include bolus obstruction and there are few instances of anaemia or calcium or vitamin deficiencies. Other complications associated with the operative procedure include leakage, stenosis, ulcer, incisional hernia, wound infection, staple-line disruption, pouch dilatation and band erosion.

Laparoscopic versus open procedures

Laparoscopic surgery has become a major advance for bariatric surgery. The learning curve is long, the technique is challenging, and there may be differences in open and laparoscopic versions of particular procedures. Nevertheless,

gastric banding, gastric bypass, vertical banded gastroplasty and sleeve gastrectomy procedures are increasingly undertaken laparoscopically. This decreases the time spent in hospital and the recovery time for the patient. In the current review comparisons of laparoscopic and open procedures have been included.

Place in the treatment pathway

As noted in the Current service provision section, bariatric surgery for morbid obesity is usually only considered after patients have attempted other forms of weight loss such as behaviour change, increased physical activity and drug therapy, but without achieving permanent weight loss. The exception to this is adults with a BMI of more than 50 where NICE guidelines recommend bariatric surgery as a first-line option (instead of lifestyle interventions or drug treatment) if surgical intervention is considered appropriate. The NICE guideline indicates that patients being considered for surgery should receive intensive management in a specialist obesity clinic. These clinics offer a combination of interventions, including drug therapy, VLCDs and sometimes psychologist input as well as surgery. An NAO report[24] cites an unpublished survey carried out by the NHS Clinical Obesity Group in 1998. This identified 12 obesity clinics in England, eight of which were run by physicians and four by surgeons. In addition, four physicians and 28 surgeons in England were seeing patients for their obesity outside obesity clinics. These data are now 10 years out of date and expert opinion suggests that there are many more specialist obesity clinics now. The British Obesity Surgery Patients Association (BOSPA) website provides a UK surgery directory which in June 2008 listed NHS hospitals in about 50 English and Welsh towns and cities where a surgeon can be contacted regarding referral for NHS bariatric surgery. In addition, contact details are provided for surgeons who only undertake private practice work.

Following surgery, patients require ongoing dietary advice and support. Those who have had an adjustable gastric band fitted will need access to a band adjustment service.

Current usage in the NHS

A recent assessment of obesity surgery in England between 1996 and 2005 found that the rate of obesity surgery had risen from 72 procedures in 1996 to 347 procedures in 2004 (equivalent to a rate of seven per million population).[67] Additional information[68] published alongside the NICE obesity guideline included results of a survey of surgeons performing bariatric surgery in England in 2006 (survey by BariatricEdge, a division of Ethicon Endo Surgery: a Johnson & Johnson company, unpublished data). This survey estimated that the total average rate of bariatric surgery was 6.5 per 100,000 population, of which around three per 100,000 population were funded by the NHS. Both the published study[67] and the unpublished survey reported variable levels of bariatric surgery occurring in different parts of the country, but these variations did not mirror regional differences in estimated levels of morbid obesity. This suggests that the intervention is not uniformly available across the country and there may be inequalities in service delivery.

BOSPA[69] have undertaken an audit of the criteria that PCTs use to approve funding for surgery. In June 2008 more than half of the 151 PCTs listed were basing their funding decisions on NICE criteria, but more than a fifth of the PCTs were using criteria that were more stringent than the NICE criteria and information was not available for a further fifth of the PCTs listed. A minority of PCTs use criteria that are not based on a particular BMI.

Expert opinion indicates that in addition to inequalities in availability of bariatric surgery, band adjustment services are also not uniformly available across the country.

Anticipated costs associated with intervention

Bariatric surgery is a highly specialised and low volume activity and is not included in the NHS Reference Costs returns. Costings developed for this review estimate the cost of the surgical procedures alone at £6985 for laparoscopic gastric bypass and £4304 for laparoscopic adjustable gastric banding. Approximately £1200 to £2000 of these costs are associated with high-cost consumables (including staples used in gastric bypass procedures and the gastric bands, and a range of single-use equipment). In addition to the procedure costs the estimate for costs of preoperative assessments is £1114, while postdischarge care of surgical patients will cost up to £1800 in the two years following gastric bypass surgery and up to £1900 following gastric banding (if costs of band fill and adjustments are included). Overall the anticipated costs for laparoscopic

gastric bypass are £11,462 and for laparoscopic adjustable gastric banding are £8762. These overall costs include estimates of additional resource use arising from adverse events during the initial hospitalisation, reoperations within two years for patients whose initial surgery was unsuccessful, abdominal hernia procedures and additional cholecystectomies in patients within two years of a bariatric procedure.

The cost estimates developed for this review may not reflect the scarcity of surgeons with appropriate training and experience to perform bariatric procedures. The previous review[15] developed a scenario to assess the impact of involving surgeons at an early stage of the learning curve – the likely impacts that directly affect treatment costs were identified as being reflected in longer operating times (50% higher), a doubling in revision rates. Including these effects raises the estimated cost of gastric bypass surgery to £14,787 (of which the procedure cost is £8795), while the estimated cost of adjustable gastric banding increases to £11,310 (of which £5510 is the procedure cost). Additional impacts of involving less experienced surgeons, that are not directly reflected in cost estimates, were identified in an increased risk of surgical mortality and a likelihood of poorer outcomes (in terms of percentage weight loss following surgery).

Rationale for this study

The prevalence of obesity (BMI > 30) and morbid obesity (BMI ≥40) among adults is increasing. A similar pattern of increasing prevalence of obesity is seen in children and young people. A systematic review and economic evaluation of surgery for morbid obesity was conducted in 2002[15] and it found that although surgery appeared effective in terms of weight change, there was limited evidence addressing the long-term consequences and its influence on the QoL of patients. The economic evaluation was based on several assumptions because of the limitations of the data available, and

it found that surgery offered additional quality-adjusted life-years (QALYs) at an additional cost when compared with non-surgical management over a 20-year period, but comparison of the different procedures suggested that the difference in cost per QALY was less clear. The review found that there were few economic evaluations comparing the different surgical interventions, and the availability of costing and resource-use data was limited. The systematic review of clinical effectiveness was also published as a Cochrane review[70] which was updated in 2005,[71] when further trials were identified, but an economic evaluation was not undertaken.

The earlier reviews[15,70,71] identified needs for further research. There was a need for good-quality randomised controlled trials (RCTs) comparing either surgery with non-surgical interventions, or comparing one type of surgical procedure with another surgical procedure. Further key implications for research were the need for an assessment of outcomes over longer time periods (at least five years) and the need to include QoL outcomes. Further good quality economic evaluations were also needed.

An update of the systematic review and economic evaluation is therefore required which will include data from more recent trials, including any that may have assessed new bariatric surgical techniques. Any good-quality research that has assessed bariatric surgery for young obese people will be considered for inclusion in the review because some current guidelines[9,64] do not rule out surgical intervention for young people. Furthermore the updated review will include people with lower BMIs than the previous reviews[15,72] (BMI > 30), to take account of the emerging literature that possible benefits of early intervention (particularly in reducing obesity-related comorbidity) outweigh the potential harms. This is reflected in one guideline[64] that allows for surgery in people with a BMI greater than 30 and serious comorbid disease.

Chapter 2
Definition of the decision problem

Decision problem

Obesity is associated with increased morbidity and mortality. Bariatric (weight loss) surgery for obesity is considered when other treatments have failed. The aim of this health technology assessment is to assess the clinical effectiveness and cost-effectiveness of bariatric surgery in the obese. This report is an update of a previously published systematic review and economic evaluation.[15,70,71] To ensure that the systematic review remains relevant to current practice, some small changes have been made to the eligibility criteria at each update. The changes made to the eligibility criteria for this update are discussed below.

Population including subgroups

The original review was restricted to adults aged 18 years or over with BMI greater than 40 or BMI greater than 35 with serious comorbid disease.[15,70,71] The present review has been broadened to include people of all ages undergoing surgery for obesity, in order to reflect some current guidelines which do not rule out surgical intervention in young people[9,64] and indications from the literature that weight loss surgery is undertaken in young people under 18 years of age. The present review also includes people with a BMI greater than 30 with serious comorbid disease, again to reflect changing guidelines from the American Society for Bariatric Surgery[64] and emerging literature suggesting that benefits may outweigh the harms in this group.

People with a BMI 30 to 35 do not meet the current NICE guideline for bariatric surgery,[9] therefore this subgroup will be considered separately where appropriate and if data allow. A further subgroup of people with BMI greater than 50 (super-obese) will also be considered separately where appropriate.

Interventions

Surgical procedures in current use are included, such as gastric bypass, biliopancreatic diversion sleeve gastrectomy, vertical banded gastroplasty and adjustable gastric banding. Four procedures that are not in current use have been excluded:

- Jejunoileal bypass was included in the original review,[15] but was excluded from the Cochrane reviews[70,71] and the present update because this procedure is not in current practice as a result of unacceptably high morbidity and mortality. Three studies (seven publications) of jejunoileal bypass that were included in the original review[15] were excluded from later updates[70,71] and the present review.
- Horizontal gastroplasty was included in the previous versions of this review.[15,70,71] However, this surgical intervention is not currently practiced and the most recent trial was published over 20 years ago. Seven studies (13 publications) of horizontal gastroplasty were therefore excluded from this update.
- One study included in previous versions of this review assessed vertical gastroplasty that was not banded.[15,70,71] This intervention has also been excluded because it is no longer practiced.
- Non-adjustable gastric banding. One study published as an abstract only[73] and included in the Cochrane reviews[70,71] included a non-adjustable gastric band as one of three interventions assessed. All bands in current use are adjustable so this arm of the trial has been excluded from the current review. The surgical cohort of the Swedish Obese Subjects (SOS) study includes a minority of participants who received either adjustable or non-adjustable gastric bands. However, this study is included in the current review because those who received gastric banding of any type make up less than a fifth of the surgical cohort and much of the data are reported for the surgical cohort as a whole.

Relevant comparators

As bariatric surgery is usually an intervention of last resort when all other methods have failed, much of the published evidence reports comparisons between one type of bariatric surgery and another.

It is anticipated that there will be few RCTs comparing surgery with no surgery (no treatment, medical management, e.g. VLCD or drugs such as orlistat or sibutramine or usual care), therefore prospective cohort studies are also included for these comparisons. Open surgery compared with laparoscopic surgery for the same procedure is also assessed. Comparisons of variations of surgical techniques rather than different procedures are excluded.

Outcomes

The primary outcomes of interest are measures of weight change, QoL, perioperative and postoperative mortality and morbidity, change in obesity-related comorbidities, and cost-effectiveness. It will be necessary to identify the resource implications of interventions and comparators, for example time in surgery, because these factors will help to inform the economic model. It is anticipated that the principal outcome of the economic model will be expressed in terms of incremental cost per QALY gained.

Overall aims and objectives of assessment

The aim of this report was to assess the clinical effectiveness and cost-effectiveness of bariatric surgery for obesity by updating and expanding the previous systematic review and economic evaluation of surgery for morbid obesity.[15,70,71]

The objectives were to:

- summarise the evidence of clinical effectiveness and cost-effectiveness of surgery when compared with no surgery (medical management, usual care or no treatment)
- summarise the evidence of clinical effectiveness and cost-effectiveness comparing different surgical procedures in current use
- develop, where appropriate, an economic model adapting an existing cost-effectiveness model or constructing a new model using best available evidence to determine cost-effectiveness in the UK
- identify priorities for future research.

Chapter 3

Methods for the systematic review of clinical effectiveness and cost-effectiveness

This report is an update of a previously published systematic review and economic evaluation.[15,70,71] The a priori methods for systematically reviewing the evidence of clinical and cost-effectiveness are described in the research protocol (Appendix 1). The protocol was sent to experts for comment; although helpful comments were received relating to the general content of the research protocol, there were none that identified specific problems with the methods of the review. The methods outlined in the protocol are briefly summarised below.

Search strategy

The search strategy for the update review was refined by an experienced information scientist. Separate searches were conducted to identify studies of clinical effectiveness, cost-effectiveness, QoL, resource use/costs and epidemiology/natural history. Sources of information and search terms are provided in Appendix 2, and a flow chart of identification of studies can be seen in Appendix 3. The most recent search was carried out in August 2008.

Searches for clinical effectiveness and cost-effectiveness literature were undertaken from the date of the last search of the previous review.[71] Electronic databases searched included: 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 databases; BIOSIS; and databases listing ongoing clinical trials. A total of 17 electronic resources were searched: 12 resources (encompassing 15 databases) listing published papers and abstracts and five databases listing ongoing clinical studies. Searches were not restricted by language and conference abstracts were not excluded from the search strategy (see Inclusion criteria section, this chapter, for inclusion criteria on language and

conference abstracts as these differed between the reviews of clinical effectiveness and cost-effectiveness studies). Bibliographies of related papers were screened for relevant studies, and the expert advisory group was also contacted for advice and peer review, and to identify additional published and unpublished references.

Inclusion and data extraction process

Titles and abstracts identified by the search strategy for the clinical effectiveness section of the review were assessed for possible eligibility by two reviewers independently. The full texts of relevant papers were then obtained and inclusion criteria were again applied by two reviewers independently using a standardised form. Any disagreements over eligibility were resolved by consensus or by recourse to a third reviewer. Data were extracted by one reviewer using a standardised data extraction form and independently checked by two further reviewers.

Titles and abstracts identified by the search strategy for the cost-effectiveness section of the review were assessed for potential eligibility by two health economists. Economic evaluations were considered for inclusion if they reported both health-service costs and effectiveness, or presented a systematic review of such evaluations. Full papers were formally assessed by one health economist with respect to their potential relevance to the research question.

Quality assessment

Within the clinical effectiveness section of the review the quality of included cohort studies was assessed using criteria recommended by NHS Centre for Reviews and Dissemination (CRD)[74] (Appendix 4). RCTs were assessed using the Cochrane criteria for judging risk of bias (Appendix 4).[75] 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.

Quality criteria were applied independently by two reviewers. At each stage, any differences in opinion were resolved through discussion or consultation with a third reviewer.

For the cost-effectiveness section of the review the included studies were summarised and critically appraised by two health economists to identify:

- the number and characteristics of alternative surgical interventions included in economic evaluations
- the choice of a comparator treatment
- population to whom the results of the economic evaluations apply
- approach and assumptions used in decision analytic models
- methods used in transforming clinical and economic data to the needs of economic modelling
- methods of dealing with uncertainties and potential bias in estimated results
- other issues as recommended by the checklist for economic evaluation publications (Drummond and Jefferson[76]) and the guidelines for good practice in decision-analytic modelling in health technology (Phillips and colleagues[77]).

Inclusion criteria

The eligibility criteria for the systematic review of clinical effectiveness differ slightly from those of the previously published versions of the review;[15,70,71] these differences are described in Chapter 2, Decision problem section. The inclusion criteria for the present review are described below.

Patients

- Adult patients fulfilling the standard definition of obese, i.e. people with a BMI of 30 or over.
- Young people who fulfil the definition of obesity for their age, sex and height.

- Where data were 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.

Interventions

- Open and laparoscopic bariatric surgical procedures in widespread current use. Clinical experts were consulted to ensure that the included procedures are those which are most relevant to current clinical practice. The procedures included are gastric bypass, biliopancreatic diversion (including biliopancreatic diversion with duodenal switch), sleeve gastrectomy, adjustable gastric banding and vertical banded gastroplasty.

Comparators

- Surgical procedures in current use in comparison with one another.
- Open surgery compared with laparoscopic surgery for the same procedure.
- Surgical procedures in current use compared to non-surgical interventions. These non-surgical interventions may have included drugs such as orlistat and sibutramine, dietary interventions, exercise and combinations of non-surgical interventions such as diet and exercise, or no surgery.

Outcomes

- To be included, studies must have reported outcomes following a minimum of 12 months of follow-up.
- Included studies had to have reported on at least one of the following outcomes: measures of weight change, QoL, perioperative and postoperative mortality and morbidity, change in obesity-related comorbidities, cost-effectiveness (i.e. both costs and outcomes should be reported). For cost-effectiveness, intermediate outcomes (in BMI) had to have been converted to final outcomes [i.e. either life-years (LYs) or QALYs], cost-effectiveness studies where results were reported only with respect to intermediate outcomes other than BMI (e.g. cost per kg of excess weight loss; cost per adverse event avoided) were not eligible for inclusion.

Types of studies

- Systematic review of clinical effectiveness: RCTs were eligible for inclusion. For the comparisons of surgical procedures with non-surgical procedures controlled clinical trials and prospective cohort studies (with a control cohort) were also eligible for inclusion (because it was anticipated that few or no RCTs would be found).
- Systematic review of cost-effectiveness: full cost-effectiveness analyses, cost–utility analyses, cost–benefit analyses and cost–consequence analyses. Only publications in English were eligible for inclusion in the systematic review of cost-effectiveness.
- Studies published as abstracts or conference presentations were eligible for inclusion in the clinical effectiveness section if sufficient details were presented to allow an appraisal of the methodology and the assessment of results to be undertaken. Conference abstracts were not eligible for inclusion in the cost-effectiveness section.

Data synthesis

Data were synthesised through a narrative review with tabulation of results of all included studies. Full data extraction forms are presented in Appendix 5 to Appendix 15. Within the clinical effectiveness section studies using similar surgical procedures were grouped together to aid interpretation. However, within these groupings there may be differences in procedures, such as modifications of procedures (for example variations of gastric bypass), or open or laparoscopic procedures. These are noted where appropriate. It was not considered appropriate to combine the included RCTs in a meta-analysis because of the heterogeneity in the patient groups, comparator treatments and outcomes (see Chapter 4, Assessment of clinical effectiveness and Chapter 7 Strengths and limitations of the assessment).

Chapter 4
Clinical effectiveness

Quantity and quality of research available

Studies identified

As this report is an update of a systematic review and economic evaluation originally published in 2002,[15] with the review of clinical effectiveness updated for the Cochrane Library in 2003[70] and 2005,[71] searching and screening have been conducted on a number of occasions. Moreover, each version update differs slightly in the studies included as the review has evolved. Appendix 3 explains how the review has evolved and notes the main differences between the reviews with respect to the eligibility criteria and studies included in each publication. A flow chart of the identification of studies at each stage can also be seen in Appendix 3.

In summary, a total of 5386 references were identified through the previous and current searches. Twenty-six studies reported in 52 publications met the current inclusion criteria.

Assessment of inter-rater agreement

Inter-rater agreement for study selection was excellent (Cohen's kappa = 0.84). Initial disagreements were resolved though discussion in all cases.

Excluded studies

The reasons for excluding 32 studies after examination of the full papers from the 2005 and 2008 updated searches can be seen in Appendix 16. Studies excluded from the original searches have been described previously.[15,70] Studies were often excluded for more than one reason, but the most common reason for exclusion was a study design other than an RCT for comparisons of surgical procedures, or a controlled prospective cohort study for comparisons of surgery versus non-surgical management. Four studies published as abstracts only were excluded because of inadequate length of follow-up.[78–81] The authors of these trials were contacted to determine if further follow-up was available, but no replies were received.

Characteristics of included studies

Twenty-three of the 26 included studies were RCTs. One study (SOS) was a prospective multicentre cohort study with matched concurrent controls. This study has multiple publications, 20 of which have been included in this review.[82–101] Throughout the review, this study will be referred to as the SOS study, with specific references cited where appropriate. Two studies had prospective cohort designs (Stoeckli and colleagues[102–104] and Buddeberg-Fischer and colleagues[105]). Two of the included studies were reported as abstracts only.[73,106] *Table 12* summarises the comparisons identified by the searches.

Participants

Most studies included participants with morbid obesity, and where this was described further, a definition of BMI greater than 40 was commonly used, often with the additional criteria of BMI greater than 35 or 37 with comorbid disease (*Table 13*). However, Angrisani and colleagues[107] included participants with BMI greater than 35, and the SOS study included men and women with a BMI greater than or equal to 34 and 38 respectively. A maximum of BMI of 50, [107,108,109,110,111] 55,[112] or 60[113,114] was also specified by some studies.

Three studies included participants notably different from the rest of the studies in this review; with two studies focusing on the lower side of the obesity continuum, and one focusing on the upper side. O'Brien and colleagues[115,116] included participants with a BMI of 30 to 35 (Class I obesity) and identifiable comorbidities. Dixon and colleagues[117] limited inclusion to people diagnosed with Type 2 diabetes and a BMI of 30 to 40. At the other extreme, Bessler and colleagues[118] required participants to have a BMI greater than 50.

The individual study sample size ranged from 20[102–104] to 4047 (SOS study); however, the number of participants included in the analysis of the SOS study depended on the length of follow-up which varied for the different outcomes reported in different publications.

The majority of participants in the studies were female, the proportion of female participants in studies ranged from 53% to 94% where reported.

TABLE 12 *List of identified comparisons*

Comparison[a]	Study
Surgery vs non-surgical interventions (RCTs and prospective cohort studies)	
Laparoscopic adjustable gastric banding vs conventional therapy[117] OR Intensive medical programme[115,116] OR No surgery[102–104] (vs open gastric bypass[102–104])	1. Dixon *et al*., 2008,[117] RCT; 2. O'Brien *et al*., 2006,[115,116] RCT; 3. Stoeckli *et al*., 2004,[102–104] Cohort study
Biliopancreatic diversion vs diet	1. Mingrone *et al*., 2002,[119] RCT
Surgery (various) vs conventional treatment[83–90]	1. SOS 1997 to 2007,[82–101] Cohort study; 2. Buddeberg-Fischer *et al*., 2006,[105] Cohort study
Comparisons of different surgical procedures (RCTs)	
Gastric bypass vs vertical banded gastroplasty	1. Howard *et al*., 1995[120]; 2. VanWoert *et al*., 1992[106]; 3. MacLean *et al*., 1995[121,122]; 4. Sugerman *et al*., 1987[123]; 5. Lee *et al*., 2004[124]; 6. Olbers *et al*., 2005[108,109]; 7. Agren and Naslund, 1989[73,b]
Gastric bypass (non-banded) vs banded gastric bypass	1. Bessler *et al*., 2007[118]
Laparoscopic gastric bypass vs laparoscopic adjustable gastric banding	1. Angrisani *et al*., 2007[107]
Laparoscopic Roux-en-Y gastric bypass vs laparoscopic sleeve gastrectomy	1. Karamanakos *et al*., 2008[125]
Vertical banded gastroplasty vs adjustable gastric banding	1. Nilsell *et al*., 2001[126]; 2. Morino *et al*., 2003[110]; 3. van Dielen *et al*., 2005[127,128]
Laparoscopic adjustable gastric banding vs laparoscopic isolated sleeve gastrectomy	1. Himpens *et al*., 2006[129]
Open gastric bypass vs laparoscopic gastric bypass	1. Puzziferri *et al*., 2006[113,114]; 2. Lujan *et al*., 2004[130]; 3. Westling and Gustavsson, 2001[131]; 4. Sundbom and Gustavsson, 2004[112]
Open vertical banded gastroplasty vs laparoscopic vertical banded gastroplasty	1. Davila-Cervantes *et al*., 2002[111]
Open adjustable silicone gastric banding vs laparoscopic adjustable silicone gastric banding	1. de Wit *et al*., 1999[132]

RCT(s), randomised controlled trial(s); SOS, Swedish Obese Subjects.
a   Note: studies may vary in technique or procedure within these groupings.
b   The study by Agren and Naslund, 1989,[73] includes a third arm, gastric banding (not adjustable), which has been reported in previous versions of this review.[70,71] However, because non-adjustable gastric bands are no longer used this comparison is not included in the current review.

Mean age ranged from 31 years in one arm of the RCT by Karamanakos and colleagues[125] to 49 years in the SOS study (*Table 13*). Excluding the three studies with notably different inclusion criteria, mean baseline BMI ranged from 37 in the RCT by Himpens and colleagues[129] (inclusion criteria were not reported by this study) to 52 in the study by vanWoert and colleagues.[106] Baseline BMI in the study focusing on Class I obesity was 34 in each group,[115,116] and was 37 in each group in the study focusing on Type 2 diabetes.[117] The study by Bessler and colleagues,[118] which focused on

participants with BMI greater than 50, had a mean baseline BMI of 59.4 in the banded gastric bypass group and 59.7 in the non-banded group.

Baseline characteristics were similar between groups in most of the studies. However, the SOS study involved an interval of about nine months between matching of controls and the start of treatment (surgery) that led to significant differences in weight and other possible risk factors. The surgical group were younger than controls, had a higher prevalence of hypertension,

and had increased BMI, blood pressure and energy intake at the time of surgery. The authors state that dissimilarities between groups at inclusion were adjusted for in the calculations. Sundbom and Gustavsson[112] stated that groups were well matched for age, sex, BMI, previous abdominal surgery and comorbid conditions; however, comorbidity appears to be higher in the open surgery group. Patients in the study by Karamanakos and colleagues[125] had a statistically significant difference in mean age between groups {37 years [standard deviation (SD 8.25)] versus 30.6 years (SD 7.8), $p = 0.023$}.

Interventions

The included studies compared a variety of interventions, which are summarised in *Table 12* and displayed visually in *Figure 1*. Although these studies have been grouped according to the type of surgery for the purposes of this systematic review, there may be variations in surgical technique or procedure within the groupings. Three RCTs and three cohort studies (one cohort study had three arms) compared surgery with non-surgical

interventions. The remaining 20 RCTs compared different surgical procedures, including various types of gastric bypass, vertical banded gastroplasty, adjustable gastric banding and isolated sleeve gastrectomy, performed with open or laparoscopic surgery. Gastric bypass (usually Roux-en-Y gastric bypass) and vertical banded gastroplasty were the most commonly investigated procedures and formed the majority of the evidence base. Comparisons of open versus laparoscopic surgery for gastric bypass (four RCTs), vertical banded gastroplasty (one RCT) and adjustable gastric banding (one RCT) were also assessed.

Outcomes

Several different measures of weight change were reported by the studies, namely BMI, change in BMI, weight, weight loss, per cent weight loss, per cent excess weight loss, fat mass, fat free mass, per cent ideal body weight and proportion of 'successes'. Some of the studies did not report measures of variability such as confidence intervals or standard deviations.
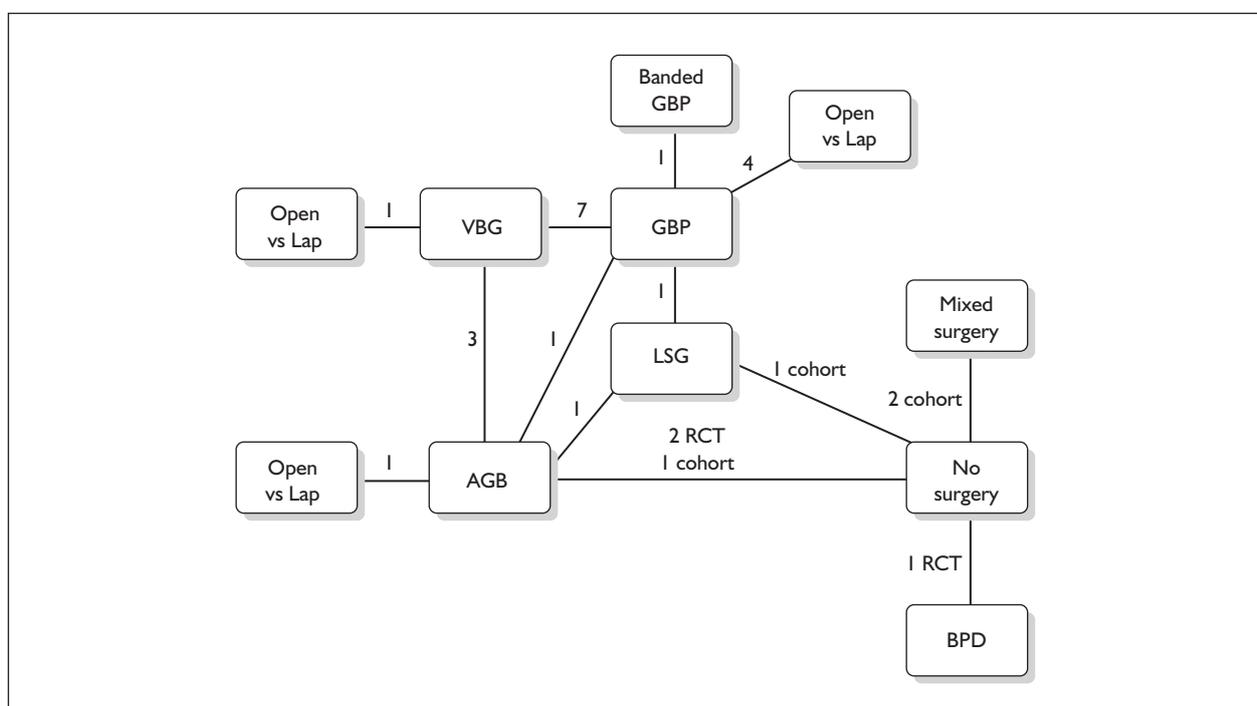

FIGURE 1 *Network of comparisons of surgical interventions for obesity. Note: The lines between interventions represent comparisons (either trials or pairs of trial arms where a study has compared more than two procedures). The numbers along the lines indicate the number of trials (or pairs of trial arms) for that comparison. Trials are RCTs unless otherwise stated. AGB, adjustable gastric banding; BPD, biliopancreatic diversion; GBP, gastric bypass; lap, laparoscopic surgery; LSG, laparoscopic sleeve gastrectomy; open, open surgery; RCT, randomised controlled trial; VBG, vertical banded gastroplasty.*

TABLE 13 *Characteristics of included studies*

Study details	Intervention	Target population and selected baseline characteristics (mean and SD unless stated otherwise)
Surgery versus non-surgical interventions (RCTs and prospective cohort studies)		
Dixon, 2008[117] Australia RCT, follow-up: 24 months	1. LAGB (*n* = 30) 2. Con therapy (*n* = 30)	*Target pop:* Type 2 diabetes, BMI 30–40, age 20–60 years AGE, years: LAGB 46.6 (7.4); con therapy 47.1 (8.7) SEX (M : F): LAGB 15 : 15, con therapy 13 : 17 BMI: LAGB 37.0 (2.7); con therapy 37.2 (2.5)
O'Brien, 2006[115,116] Australia RCT, follow-up: 24 months	1. LAGB (*n* = 40) 2. Intensive non-surgical programme (*n* = 40)	*Target pop:* BMI 30 to 35 with comorbidities, age 20–50 years AGE, years: LAGB 41.8 (6.4); non-surgical 40.7 (7.0) SEX (M : F): LAGB 10 : 30; non-surgical 9 : 31 BMI: LAGB 33.7 (1.8); non-surgical 33.5 (1.4)
Mingrone, 2002[119] Italy RCT, follow-up: 1 year	1. BPD (*n* = 46) 2. Diet (*n* = 33)	*Target pop:* morbidly obese AGE, years: 30–45 SEX (M : F): BPD 15 : 31, diet 12 : 21 BMI: women, diet 48.4 (8.9), BPD 48.3 (6.3). men, diet 47.8 (8.8), BPD 48.0 (5.4)
SOS, 1997 to 2007[82–101] Sweden Multicentre, cohort study, follow-up: up to 10 years	1. Surgery (VBG, Gband or GBP) (*n* = 2010) 2. Controls: conventional treatment, not standardised, best non-surgical options available at the time (*n* = 2037)	*Target pop:* BMI ≥34 (men) and ≥38 (women), 37–60 years AGE, years: surgery 47.2 (5.9), control 48.7 (6.3) SEX: (M : F) surgery 590 : 1420, control 590 : 447 BMI: surgery 42.4 (4.5), control 40.1 (4.7) (all data here taken from most recently published study)
Stoeckli, 2004[102–104] Switzerland Cohort study, follow-up: 24 months	1. LAGB (*n* = 8) 2. Open RYGBP (*n* = 5) 3. Control (*n* = 7)	*Target pop:* morbid obesity (BMI > 37) AGE, years (SE): LAGB 41.1 (2.6), RYGBP 43.8 (4.4), controls 49.9 (2.6) SEX (M : F): LAGB 2 : 6, RYGBP 0 : 5, controls 2 : 5 BMI: LAGB 41.7 (1.0), RYGBP 43.6 (2.0), controls 41.1 (1.0)
Buddeberg-Fischer, 2006[105] Switzerland Cohort study Mean follow-up 3.2 years (SD 1.3, range 0.28–5.8)	1. Surgery (LAGB, LRYGBP) (*n* = 63) 2. No surgery (*n* = 30)	*Target pop:* BMI > 40, or > 35 with substantial comorbidity AGE, years 43.5 (9.8, range 21.65) SEX (M : F) 23 : 70 BMI: surgery, 44.7 (6.1) [LRYGBP (*n* = 23), 47.3 (7.8); LAGB (*n* = 40), 43.4 (4.5)]; no surgery 42.9 (5.5)
Comparisons of different surgical procedures (all RCTs)		
Howard, 1995[120] USA Follow-up: 12 to 78 months	1. GBP (*n* = 20) 2. VBG (*n* = 22)	*Target pop:* Class IV obesity (BMI > 40); < 50 years old AGE, years: GBP 38.1 (SE 1.9), VBG 36.5 (SE 2.3) SEX (M : F): GBP 5 : 15, VBG 4 : 18 BMI: not reported
VanWoert, 1992[106] USA (abstract) Follow-up: 36 months	1. GBP (*n* = 15) 2. VBG (*n* = 17)	*Target pop:* BMI > 40 AGE, years: GBP 38 (8), VBG 38 (10) SEX (M : F): GBP 4 : 11, VBG 3 : 14 BMI: GBP 52 (SD 10), VBG 51 (SD 6)
MacLean, 1995[121,122] Canada Follow-up: up to 6.5 years	1. VBG (*n* = 54) 2. RYGBP (*n* = 52)	*Target pop:* target population not stated AGE, years: VBG 38.8 (9.5), RYGBP 40.1 (7.7) SEX: not reported BMI: VBG 48.2 (6.5), RYGBP 49.9 (7.4)

TABLE 13 *Characteristics of included studies (continued)*

Study details	Intervention	Target population and selected baseline characteristics (mean and SD unless stated otherwise)
Sugerman, 1987[123] USA Follow-up: 3 years	1. RYGBP ($n = 20$) 2. VBG ($n = 20$)	*Target pop:* more than 100 lb (45.5 kg) above ideal weight AGE, years: RYGBP 38 (11), VBG 38 (9) SEX (M:F): RYGBP 2:18, VBG 2:18 BMI: not reported
Lee, 2004[124] Taiwan Follow-up: Mean 20 months (range 18 to 30)	1. LVBG ($n = 40$) 2. LRYGBP ($n = 40$)	*Target pop:* significant obesity > 5 years, BMI > 40 or BMI > 35 with comorbidities, age 18–59 AGE, years: LVBG 32.5 (7.8), LRYGBP 31.6 (8.6) SEX (M:F): LVBG 11:29, LRYGBP 13:27 BMI: LVBG 43.14 (6.1), LRYGBP 43.18 (7.5)
Olbers, 2006[108,109] Sweden Follow-up: 24 months	1. LRYGBP ($n = 37$) 2. LVBG ($n = 46$)	*Target pop:* BMI > 40 or > 35 with obesity-associated morbidity, BMI < 50 AGE (median, range), years: LRYGBP 37 (34–61); LVBG 34 (26–60) SEX (M:F): LRYGBP 12:25; LVBG 10:36 BMI: LRYGBP 42.7 (4.0); LVBG 42.1 (4.2)
Agren and Naslund, 1989[73] Sweden Follow-up: 18 months	1. VBG ($n = 27$) 2. Loop GBP ($n = 25$)	*Target pop:* morbidly obese AGE: not reported SEX: not reported BMI 42.8
Bessler, 2007[118] USA Follow-up: up to 36 months	1. Banded long-limb GBP ($n = 46$) 2. Non-banded long-limb GBP ($n = 44$)	*Target pop:* BMI > 50 AGE, years: banded GBP 40.6 (7.4); non-banded GBP 42.6 (7.2) SEX (M:F): banded GBP 20:26; non-banded GBP 12:32 BMI: banded GBP 59.4 ± 7.3; non-banded GBP 59.7 ± 7.1
Angrisani, 2007[107] Italy Follow-up: 60 months	1. LRYGBP ($n = 24$) 2. LAGB ($n = 27$)	*Target pop:* BMI > 35 to < 50, age > 16 years but < 50 years AGE, years: LRYGBP 34.1 (8.9); LAGB 33.8 (9.1) SEX (M:F): LRYGBP 4:20; LAGB 5:22 BMI (range): LRYGBP 43.8 ± 4.1 (38.9–48.9); LAGB 43.4 ± 4.2 (38.1–49.2)
Nilsell, 2001[126] Sweden Follow-up: 4–5 years	1. AGB ($n = 29$) 2. VBG ($n = 30$)	*Target pop:* BMI > 40 or BMI > 37 with obesity associated comorbidity AGE, years: AGB 38 (20–58), VBG 39 (19–59) SEX (M:F): AGB 8:21, VBG 6:24 BMI: AGB 42.8 (5.4), VBG 43.9 (3.8)
Morino, 2003[110] Italy Follow-up: mean 33.1 months (range 24–46)	1. LAGB ($n = 49$) 2. LVBG ($n = 51$)	*Target pop:* BMI 40–50, aged 18–60 years AGE, years: LAGB 37.2 (20–55), LVBG 38.2 (21–58) SEX (M:F): LAGB 11:38, LVBG 8:43 BMI: LAGB 44.7 (40.1–50.0), LVBG 44.2 (40.0–50.0)
van Dielen, 2005[127,128] The Netherlands Follow-up: 24 months and 84 months	1. Open VBG ($n = 50$) 2. LAGB ($n = 50$)	*Target pop:* BMI > 40 or > 35 with comorbidities; age 18–60 years AGE: VBG 39 (8.5) years; LAGB 37.2 (9.7) years SEX (M:F): Open VBG 10:40; LAGB 10:40 BMI: VBG 46.6 (6.4); LAGB 46.7 (6.1)

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TABLE 13 *Characteristics of included studies (continued)*

Study details	Intervention	Target population and selected baseline characteristics (mean and SD unless stated otherwise)
Karamanakos, 2008[125] Greece Follow-up: 1 year	1. LRYGBP (*n* = 16) 2. LSG (*n* = 16)	*Target pop:* not reported AGE, years: LRYGBP 37 (8.25), LSG 30.6 (7.8), *p* = 0.023 SEX (M:F): LRYGBP 4:12, LSG 1:15 BMI: LRYGBP 46.6 (3.7), LSG 45.1 (3.6)
Himpens, 2006[129] Belgium Follow-up: 36 months	1. LAGB (*n* = 40) 2. LISG (*n* = 40)	*Target pop:* not stated AGE (median, range), years: LAGB 36 (20–61); LISG 40 (22–65) SEX (M:F): LAGB 7:33; LISG 9:31 BMI (median, range): LAGB 37 (30–47); LISG 39 (30–53)
Puzziferri, 2006[113,114] USA Follow-up: 36 months	1. LRYGBP (*n* = 79) 2. Open RYGBP (*n* = 76)	*Target pop:* BMI 40–60; age 21–60 years AGE: LRYGBP 40 years (± 8), RYGBP 42 years (± 9) SEX (M:F): LRYGBP 7:72, RYGBP 9:67 BMI: LRYGBP 47.6 (± 4.7), RYGBP 48.4 (± 5.4)
Lujan, 2004[130] Spain Follow-up: mean 23 months	1. LGBP (*n* = 53) 2. Open GBP (*n* = 51)	*Target pop:* BMI > 40 or BMI > 35 with coexisting pathologic disorders AGE, years: LGBP 37 (18–64), GBP 38 (20–63) SEX (M:F): LGBP 10:43, GBP 13:38 BMI: LGBP 48.53 (36–78), GBP 52.20 (37–80)
Westling and Gustavsson, 2001[131] Sweden (abstract) Follow-up: 1 year	1. LRYGBP (*n* = 30) 2. Open RYGBP (*n* = 21)	*Target pop:* BMI > 40 or BMI > 35 with significant comorbidity AGE overall group: 36 years (SD 9) SEX overall group: 94% female BMI LRYGBP 41 (SD 4), RYGBP 44 (SD 4)
Sundbom and Gustavsson, 2004[112] Sweden Follow-up: 1 year	1. Hand-LRYGBP (*n* = 25) 2. Open RYGBP (*n* = 25)	*Target pop:* BMI < 50. minimum BMI not reported AGE (range), years: hand-LRYGBP 37 (19–54), RYGBP 38 (24–54) SEX (M:F): hand-LRYGBP 2:23, RYGBP 3:22 BMI: hand-LRYGBP 44 (range 36–54), RYGBP 45 (range 34–54)
Davila-Cervantes, 2002[111] Mexico Follow-up: 1 year	1. Open VBG (*n* = 14) 2. LVBG (*n* = 16)	*Target pop:* BMI 40–50 AGE median (range), years: VBG 36.5 (22–56), LVBG 34.5 (24–46) SEX (M:F) VBG 1:13, LVBG 2:14 BMI median (range): VBG 43 (37–50), LVBG 45 (38–50)
de Wit, 1999[132] The Netherlands Follow-up: 1 year	1. Open AGB (*n* = 25) 2. LAGB (*n* = 25)	*Target pop:* BMI > 40, aged 18–55 years AGE: not reported SEX (M:F): LAGB 8:17, AGB 8:17 BMI: LAGB 51.3 (10.4), AGB 49.7 (5.6)

AGB, adjustable gastric banding; BMI, body mass index; BPD, biliopancreatic diversion; Con therapy, conventional therapy; GBP, gastric bypass; Hand-LRYGBP, hand-assisted laparoscopic Roux-en-Y gastric bypass; LAGB, laparoscopic adjustable gastric banding; LGBP, laparoscopic gastric bypass; LRYGBP, laparoscopic Roux-en-Y gastric bypass; LVBG, laparoscopic vertical banded gastroplasty; LSG, laparoscopic sleeve gastrectomy; LISG, laparoscopic isolated sleeve gastrectomy; open, open surgery; RYGBP, Roux-en-Y gastric bypass; RCT, randomised controlled trial; VBG, vertical banded gastroplasty.

QoL was reported by just five studies,[86,100,105,113–116,124] (three RCTs and two cohort studies) and comorbidities were reported by eight studies[88,89,97,107,113–118,127,129] (seven RCTs and one cohort study).

Mortality, adverse events and/or additional procedures were reported by most studies.

Follow-up

The minimum duration of follow-up for inclusion in this review was 12 months, and most studies followed participants for 12, 24 or 36 months. Studies with longer follow-up periods included Nilsell and colleagues[126] (four to five years), Angrisani and colleagues[107] (60 months), Howard and colleagues[120] (12 to 78 months), MacLean and colleagues[121,122] (6.5 years), van Dielen and colleagues[127,128] (24 months and 84 months). The longest follow-up was for 10 years by the SOS study (*Table 13*). It should be noted that some studies did not follow all participants for the given length of time.

Country

Six studies, including the SOS study, were conducted in Sweden[73,108,109,112,126,131] and five studies were conducted in the USA.[106,113,114,118,120,123] Three studies were conducted in Italy.[107,110,119] Two studies were conducted in each of Switzerland,[102–105] the Netherlands[127,128,132] and Australia.[115–117] One study was conducted in Belgium,[134] Canada,[121,122] Mexico,[111] Spain,[130] Taiwan[124] and Greece.[125]

Risk of bias in included studies
Randomised controlled trials

The summary of risk of bias assessment of RCTs can be seen in *Table 14*.

Allocation

Nine of 23 RCTs described adequate allocation sequence generation,[108–110,115–117,123,125,127,128,130,132] and just five had adequate concealment of allocation.[110,115,116,118,130,132] The method of allocation sequence generation and concealment was not reported by the remaining studies, therefore they were judged to be of uncertain risk of bias.

Blinding

Only one RCT reported that outcome assessors were blinded to the intervention assignment.[125] Outcome assessors were not blinded to the intervention assignments in three RCTs,[115–117,126] therefore they were judged to be at high risk of bias. This information was not reported by the remaining RCTs.

Six RCTs assessed outcomes self-reported by participants. In four of these studies participants were not blinded to the intervention received,[113–116,126,131] and in two studies blinding of participants was not reported or was unclear.[118,124]

Incomplete outcome data

Incomplete outcome data for weight loss were adequately addressed by 14 RCTs (*Table 14.3*).[107–110,112,117,119,120,123,125–129,131,132] The remaining nine RCTs were judged to be at uncertain risk of bias. The withdrawals in the study by O'Brien and colleagues[115,116] were uneven between groups, but as reasons were not provided for all withdrawals it was not clear whether withdrawals were related to outcome. In the studies by Lujan and colleagues[130] and Bessler and colleagues,[118] the number of participants included at each follow-up was not reported. The study by Puzziferri and colleagues was reported in two publications,[113,114] the most recent of which contained a smaller number of participants, but no explanation for this was given. Information in the study by MacLean and colleagues[121,122] was contradictory between tables and text. Presence or absence of missing outcome data was not reported by four studies.[73,106,124,129]

Three RCTs assessed QoL.[113–116,124] Incomplete outcome data for QoL were not reported by Lee and colleagues.[124] O'Brien and colleagues[115,116] analysed QoL data only for those who completed the study, which suffered from uneven withdrawals between the groups as previously stated. QoL in the study by Puzziferri and colleagues[113,114] was reported only for 44 of 155 patients originally randomised, with no explanation given.

Comorbidity was assessed by seven RCTs. Incomplete outcome data for comorbidity were adequately addressed by three studies,[107,117,127,128,132] but the remaining four studies were judged to be of uncertain risk of bias.[113–116,118,129]

Selective reporting

The study by Bessler and colleagues[118] was judged not to be free of selective outcome reporting, as per cent excess weight loss was reported at 6, 12, 24 and 36 months follow-up (with a statistically significant difference at 36 months), while BMI was reported at 12 and 24 months only, with no measure of variance or statistical analysis. The remaining studies were judged to be of uncertain risk of bias. For example, the studies by Agren and Naslund[73] and VanWoert and colleagues[106] are reported as abstracts only, therefore limited data were provided. Lujan and colleagues[130] reported BMI in a figure only, with no exact data reported

and no measure of variance. Mingrone and colleagues[119] did not report adverse effects.

Other potential sources of bias

Four RCTs were judged to be at high risk of bias because they used block randomisation in an unblinded trial which can mean it is possible to predict future assignments.[113,114,117,123,131] In addition, recruitment to the RCT by Sugerman and colleagues[123] was stopped early (after nine months) following an a priori stopping rule which stated that when a significant difference ($p < 0.05$) in weight loss was noted for either treatment, patient recruitment would cease until patients had achieved the same follow-up after surgery. The study would have reopened if statistical significance $p < 0.01$ was not present when all patients had reached an equivalent time frame after surgery. Studies that are stopped early are more likely to show extreme treatment effects than those that continue to the end.[135] Sundbom and Gustavsson[112] was also judged to be at high risk of bias, as there appeared to be higher comorbidity on one of the treatment arms. The remaining RCTs were judged to be of uncertain risk of bias, because there was either insufficient information to assess whether an important risk of bias exists, or insufficient rationale or evidence that an identified problem will introduce bias. For example, Olbers and colleagues[108,109] excluded 17 patients after randomisation either because they expressed a preference about the surgery they received, or were found to have a BMI > 50; the effect of the exclusion of these patients was unclear. Also, Angrisani and colleagues[107] reported that they were in the early phase of the learning curve for one intervention, whereas the senior author had more experience with the comparator.

Prospective cohort studies

The summary of quality assessment of three included cohort studies can be seen in *Table 15*. The SOS study and the study by Stoeckli and colleagues[102–104] adequately described the groups and the distribution of prognostic factors. Buddeberg-Fischer and colleagues[105] did not report baseline characteristics separately for each group, therefore it was uncertain whether the groups were comparable on all important confounding factors. Although the groups in the SOS study were not comparable on all important factors, these were adjusted for in the analysis. The groups in the study by Stoeckli and colleagues[102–104] were judged to be comparable. It was not clear in any of the studies whether the groups were assembled at a similar point in their disease progression. Outcome

assessors were not blind to the intervention in the SOS study or in the study by Buddeberg-Fischer and colleagues,[105] in which all measures, including BMI, were self-reported by participants. Blinding was not reported by Stoeckli and colleagues.[102–104] Dropout rates for each group and reasons for dropout were not reported by any of the studies.

Allocation of participants in the cohort studies

In the SOS study, participants could volunteer for conventional or surgical treatment. For each surgical case a control was matched by computer taking into account 18 variables. The study by Stoeckli and colleagues[102–104] included participants opting for surgical treatment, choosing either adjustable silicone gastric banding or gastric bypass. The control group were patients attending diet consultation, although the reasons for the patients not undergoing surgery are not given. Buddeberg-Fischer and colleagues[105] included patients applying for bariatric surgery. However, the comparability of the surgery and no-surgery groups is unclear because although one paper states that all but three participants met the criteria for surgery (one had BMI 31.6, two were aged > 60 years),[105] about nine participants in an earlier publication said that the reason for not undergoing surgical treatment was that their BMI was under the limit for morbid obesity.[133]

Missing outcome data due to participant withdrawals and losses to follow-up

Reporting of missing outcome data formed part of the quality assessment of the included studies (see Risk of bias in included studies, this chapter). Here, two factors contributing to missing outcome data within RCTs: participant withdrawals from studies, and losses to follow-up are addressed. Reporting of these factors within the RCTs included in this review was variable. Only two RCTs specifically reported on study withdrawals. In the study by Dixon and colleagues[117] one participant (3.3%) withdrew in the LAGB group and four participants (13.3%) withdrew in the conservative therapy group, leading to an overall follow-up of 55 of 60 participants (92%) at two years. O'Brien and colleagues[115,116] reported the withdrawal of one participant (2.5%) in the surgical group and five withdrawals (12.5%) from the non-surgical group, leading to an overall follow-up of 74 of 80 participants (93%) at two years. O'Brien and colleagues also reported that two (5%) participants were lost to follow-up from the non-surgical group

TABLE 14 *Summary of quality assessment of 23 RCTs*

	Adequate sequence generation?	Allocation concealment?	Blinding of outcome assessors?	Blinding of participants on self-reported outcomes?	Incomplete outcome data addressed? (weight loss)	Incomplete outcome data addressed? (QoL)	Incomplete outcome data addressed? (comorbidity)	Free of selective reporting?	Free of other bias?
Agren and Naslund, 1989[73]	?	?	?	n/a	?	n/a	n/a	?	?
Angrisani, 2007[107]	?	?	?	n/a	+	n/a	+	?	?
Bessler, 2007[118]	?	+	?	?	?	n/a	?	−	?
Davilla-Cervantes, 2002[111]	?	?	?	n/a	+	n/a	n/a	?	?
de Wit, 1999[132]	+	+	?	n/a	+	n/a	n/a	?	?
Dixon, 2008[117]	+	?	−	n/a	+	n/a	+	?	−
Himpens, 2006[129]	?	?	?	n/a	?	n/a	?	?	?
Howard, 1995[120]	?	?	?	n/a	+	n/a	n/a	?	?
Karamanakos, 2008[125]	+	?	+	n/a	+	n/a	n/a	?	?
Lee, 2004[124]	?	?	?	?	?	?	n/a	?	?
Lujan, 2004[130]	+	+	?	n/a	?	n/a	n/a	?	?
MacLean, 1995[121,122]	?	?	?	n/a	?	n/a	n/a	?	?
Mingrone, 2002[119]	?	?	?	n/a	+	n/a	n/a	?	?
Morino, 2003[110]	+	+	?	n/a	+	n/a	n/a	?	?
Nilsell, 2001[126]	?	?	−	−	+	n/a	n/a	?	?
O'Brien, 2006[115,116]	+	+	−	−	?	?	?	?	?
Olbers, 2005[108,109]	+	?	?	n/a	+	n/a	n/a	?	?
Puzziferri, 2001[113,114]	?	?	?	−	?	?	?	?	−
Sugerman, 1987[123]	+	?	?	n/a	+	n/a	n/a	?	−
Sundbom and Gustavsson, 2004[112]	?	?	?	n/a	+	n/a	n/a	?	−
Van Dielen, 2005[127,128]	+	?	?	n/a	+	n/a	+	?	?
VanWoert, 1992[106]	?	?	?	n/a	?	n/a	n/a	?	?
Westling and Gustavsson, 2001[131]	?	?	?	−	+	n/a	n/a	?	−

'+', yes (low risk of bias); '−', no (high risk of bias); '?', unclear (uncertain risk of bias); 'n/a', not applicable; QoL, quality of life.

because they moved overseas. There was therefore an overall loss to follow-up in this study of 2.5% at two years. Seven further RCTs also reported on participants lost to follow-up (*Table 16*) with these losses ranging from 1% to 9% for the overall study population. Five RCTs reported that no patients were lost to follow-up (Karamanakos and colleagues,[125] Lujan and colleagues,[130] Westling and

Gustavsson,[131] Sundbom and Gustavsson[112] and Davila-Cervantes and colleagues[111]). One RCT (Lee and colleagues[124]) states that an intention-to-treat (ITT) analysis was conducted, but it is unclear if this applied to the weight loss at two years outcome where a figure suggests less than two-thirds of the participants contribute data and no information is provided regarding patients lost to follow-up.

TABLE 15 *Summary of quality assessment of three included non-randomised studies*

Quality item	Buddeberg- Fischer, 2006[105]	SOS study	Stoeckli, 2004[102–104]
Is there sufficient description of the groups and the distribution of prognostic factors?	No	Yes – differences between groups	Yes
Are the groups assembled at a similar point in their disease progression?	Uncertain	Unclear	Uncertain
Is the intervention/treatment reliably ascertained?	Yes	Yes	Yes
Were the groups comparable on all important confounding factors?	Uncertain	No – significant differences between groups	Yes
Was there adequate adjustment for the effects of these confounding variables?	No	Yes – states adjustments made where appropriate	Not applicable
Was outcome assessment blind to exposure status?	No. All measures, including BMI, were self-reported	No	Uncertain
Was follow-up long enough for the outcomes to occur?	Yes	Yes	Yes
What proportion of the cohort was followed up?	119/131 at first follow-up, 93/131 at second follow-up.	At 2 years: 84% surgical, 93% control / At 8 years: 73% of surgical, 67% control	Uncertain
Were dropout rates and reasons for dropout similar across intervention and unexposed groups?	No	Unclear – numbers and reasons not given	Uncertain

SOS, Swedish Obese Subjects.

The number of participants contributing data is observed to decrease over time in four RCTs but no reasons are provided for this.[110,113,114,118,120] In the remaining four RCTs losses, to follow-up are not reported and it is not possible to ascertain how many patients contribute data at each follow-up time point.[73,106,119,134]

Assessment of clinical effectiveness evidence

Meta-analysis was considered inappropriate. In some cases, a comparison of surgical procedures (such as gastric bypass versus adjustable gastric banding, or adjustable gastric banding versus isolated sleeve gastrectomy) was assessed by just one study. Where the same procedures were compared by more than one RCT, there were often differences in the outcomes reported or the patient groups. The studies comparing surgery with non-surgical interventions also differed in the surgical procedures and the non-surgical comparators. Standard deviations (or any data by which to calculate them) were not reported by the majority of studies. This is discussed further in Chapter 7, Strengths and limitations of the assessment.

Surgery versus non-surgical interventions

Three RCTs and three cohort studies compared surgery with non-surgical interventions; however, the types of surgery or the comparators differed between the studies. The results below are discussed according to study design.

Weight change
Randomised controlled trials

The two RCTs that compared laparoscopic adjustable gastric banding with non-surgical interventions in obese people (BMI 40 or less) with identifiable comorbidities, reported statistically significant benefit on measures of weight change for those receiving laparoscopic adjustable gastric banding[115–117] (*Table 17*). In a comparison of laparoscopic adjustable gastric banding with non-surgical interventions in people with a BMI ranging from 30 to 35 and identifiable comorbidities, O'Brien and colleagues[115,116] reported a statistically significant ($p < 0.001$) difference in the weight of participants at 12, 18 and 24 months. While people in the laparoscopic adjustable gastric banding group consistently lost weight during the two-year follow-up, those in the non-surgical group increased in weight, despite an

TABLE 16 Withdrawals and losses to follow-up

	Study arm A	Study arm B	Overall	Other comments
Withdrawals				
Dixon, 2008[117]	LAGB: 1/30 (3.3%)	Conservative therapy: 4/30 (13.3%)	5/60 (8%) at 2 years	ITT analysis
O'Brien, 2006[115,116]	Surgical: 1/40 (2.5%)	Non-surgical: 5/40 (12.5%)	6/80 (7%) at 2 years	Lost to follow-up also reported, but no other missing data
Lost to follow-up				
O'Brien, 2006[115,116]	Surgical: 0	Non-surgical: 2/40 (5%)	2/80 (2.5%) at 2 years	Withdrawals also reported, but no other missing data
Maclean, 1995[121,122]	GBP/VBG: 1 participant (study arm not stated)		1/106 (1%) at 3 years	Other outcome data missing. Reasons not stated
Sugerman, 1987[123]	GBP: 0	VBG: 1/20 (5%)	1/40 (2.5%) at 3 years	Reasons for other missing data provided
Olbers, 2005[108,109]	LGBP: 1/37 (2.7%)	LVBG: 2/46 (4.3%)	3/83 (3.6%) at 2 years	Reasons for other missing data provided
Angrisani, 2007[107]	LAGB: 1/27 (3.7%)	LGBP: 0/24	1/51 (2%) at 5 years	States not ITT. Unclear how many participants contribute data at each time point.
Nilsell, 2001[126]	VBG: 2/30 (6.7%)	AGB: 3/29 (10.3%)	5/59 (8.5%) at 5 years	Not all participants followed up at every time point.
Van Dielen, 2005[127,128]	Open VBG	LAGB	9% at 7 years[a]	
de Wit, 1999[132]	Open AGB: 1/25 (4%)	Lap AGB: 0/25	1/50 (2%) at 1 year	

AGB, adjustable gastric banding; GBP, gastric bypass; ITT, intention to treat; LAGB, laparoscopic adjustable gastric banding; LGBP, laparoscopic gastric bypass; LVBG, laparoscopic vertical banded gastroplasty; lap, laparoscopic surgery; VBG, vertical banded gastroplasty.
a   This follow-up period reported by a recent abstract[128] was for a mean of 84 months.

initial loss of weight at six months. The differences in weight change were reflected in their respective BMIs, with statistically significant ($p < 0.001$) differences at beyond the six-month follow-up. Participants in the laparoscopic adjustable gastric banding group experienced a decrease in their BMI from 33.7 at baseline to 26.4 at two years compared with a decrease from a BMI of 33.5 at baseline to 31.5 at two years for those in the non-surgical group. By two years people receiving laparoscopic adjustable gastric banding had lost 87.2% of excess weight, statistically significantly ($p < 0.001$) more than the 21.8% lost by people in the non-surgical group. Some 98% of those people with a laparoscopic adjustable gastric banding had achieved a satisfactory weight loss (greater than 25% of excess weight loss) at two years, compared with 35% of people in the non-surgical group.

Dixon and colleagues,[117] who assessed the effectiveness of laparoscopic adjustable gastric banding and conventional therapy on obese people (BMI 30 to 40) diagnosed with Type 2 diabetes at two years follow-up, found a statistically significantly ($p < 0.001$) greater mean percentage weight loss following laparoscopic adjustable gastric banding (20.0%) compared with conventional therapy (1.4%). This equated to a statistically significant ($p < 0.001$) difference in mean weight loss with those receiving laparoscopic adjustable gastric banding losing an additional 19.6 kg. The change in weight resulted in a reduction in the mean BMI for people in the laparoscopic adjustable gastric banding group from 36.9 to 29.5, while those in the conventional therapy group declined from a BMI 37.1 to 36.6. Dixon and colleagues reported that the loss of weight represented a loss of 62.5% of excess weight (using BMI 25 as ideal weight) for people with the laparoscopic adjustable gastric banding and 4.3% for people receiving conventional therapy. Similar benefits were noted on measures of waist circumference and waist : hip ratio for those in the laparoscopic adjustable gastric banding group compared with the conventional therapy group (Appendix 5).

Mingrone and colleagues[119] randomised patients to either biliopancreatic diversion or a diet of 20 kcal/kg fat-free mass, 55% carbohydrates and 15% proteins that was modified every six months according to analysis of fat-free mass. Weight, BMI, fat-free mass and fat mass were significantly reduced in both men and women 12 months following biliopancreatic diversion compared with baseline ($p < 0.0001$). Weight loss in women and men following surgery was 35 kg and 52 kg, respectively, and 7 kg and 9 kg, respectively, following the diet. The study did not present a statistical comparison of surgery versus diet, and because the results reflect a before and after comparison only they should be treated with caution.

Cohort studies
In 3505 participants who completed two years follow-up, the SOS study reported a significantly greater weight loss among gastric surgery patients (23.4%) than for those receiving conventional treatment (0.1% gain) [difference 22.2, 95% confidence interval (CI) 21.6 to 22.8, $p < 0.001$][97] (*Table 17*). Among 1276 patients followed for 10 years, patients in the surgical group had a 16% (SD 12.1) weight loss compared with a 1.5% (SD 9.9) gain in weight for patients receiving conventional treatment. This equates to a mean reduction in weight and BMI of −19.7 kg (SD 15.8) and −6.7 (SD 5.4), respectively, for the surgical group versus a gain in weight and BMI of 1.3 kg (SD 13.8) and 0.7 (SD 4.9), respectively for the conventional treatment group, a statistically significant difference between groups ($p < 0.0001$).[100] Weight loss after 10 years was greater following gastric bypass (25%, SD 11) than following vertical banded gastroplasty (16%, SD 11) or gastric banding (adjustable or non-adjustable) (14%, SD 14), although it should be noted that this was not tested statistically and may be subject to selection bias (systematic differences between the groups) as the groups were not randomised. After 15 years, the weight loss was 27% (SD 12), 18% (SD 11) and 13% (SD 14), for the three surgical groups respectively; although it should be noted that the numbers followed for this duration were much smaller (Appendix 5).[99]

One small cohort study, reported by Buddeberg-Fischer and colleagues,[105] compared participants undergoing laparoscopic gastric banding or laparoscopic gastric bypass (surgery group) with a no-surgery control group. While mean BMI was not shown to be statistically significantly different between the two groups at end point (mean 3.2 years follow-up), the mean change in BMI was ($p < 0.001$), indicating greater BMI reduction in the surgery group (*Table 4.6*). The percentage of excess weight loss was also seen to be statistically significantly better in the surgery group compared with the no-surgery group ($p < 0.001$). It should be noted, however, that there is some potential for bias as these measures were self-reported and the rates of dropout were different between the two groups over time. The study also assessed BMI and percentage excess weight loss between the two types of surgical procedures used within the surgery arm. The study showed that the mean change in BMI was greater in those undergoing laparoscopic gastric bypass than those undergoing laparoscopic gastric banding [−27.7 (SD 12.6) versus −17.2 (SD 12.5) for the two groups respectively, $p = 0.002$], and that the percentage excess weight loss was greater in the laparoscopic gastric bypass subgroup than the laparoscopic gastric banding group [52.8% (SD 17.0) versus 36.0% (SD 24.5) respectively, $p = 0.005$] (Appendix 5). Care should be used when interpreting these results, however, because the sample sizes were small, there was some degree of crossover between surgical options, this was not a planned comparison, and the surgical groups were not randomised and therefore were subject to selection bias.

The small cohort study with just 20 participants, reported by Stoeckli and colleagues,[102–104] also found a statistically significant lower mean BMI two years following surgery [gastric bypass 32.9 (SD 6.7); laparoscopic adjustable silicone gastric banding 33.2 (SD 4.7); compared with a control group who did not undergo surgery 41.0 (SD 3.4)].

Quality of life
Randomised controlled trials
O'Brien and colleagues compared changes in the short-form health survey (SF-36) domain scores from baseline to two years follow-up for people undergoing laparoscopic adjustable gastric banding and non-surgical therapy.[115,116] Although no point estimates were reported, O'Brien and colleagues noted improvements in scores on all eight domains for the laparoscopic adjustable gastric banding group and on three domains (physical function, vitality and mental health) for the non-surgical therapy group. Statistically significantly greater improvements were reported for five of the eight domains for laparoscopic adjustable gastric banding compared with the non-surgical group (*Table 18*).

TABLE 17 *Summary of results: surgery versus non-surgical management – weight change*

Dixon, 2008[117]	LAGB (n = 30)	Con therapy (n = 30)	Effect size/p-value (95% CI)
% initial weight loss at 2 years	20.0 (± 9.4)	1.4 (± 4.9)	$p < 0.001$
% excess weight loss at 2 years	62.5	4.3	
Weight loss (kg) at 2 years	−21.1 (± 10.5)	−1.5 (± 5.4)	Difference −19.6 (−23.8 to −15.2) $p < 0.001$
Reduction in BMI at 2 years	from 36.9 to 29.5	from 37.1 to 36.6	
O'Brien, 2006[115,116]	**LAGB (n = 40)**	**Non surgical (n = 40)**	
Weight at 12 months [mean (95% CI) kg]	76.3 (74.1–78.5)	85.3 (83.0–87.5)	$p < 0.00 1$
Weight at 18 months [mean (95% CI) kg]	75.2 (73.1–77.4)	87.7 (79.9–83.0)	$p < 0.001$
Weight at 24 months [mean (95% CI) kg]	74.5 (72.4–76.7)	89.5 (80.5–83.6)	$p < 0.001$
BMI at 12 months [mean (95% CI)]	27.0 (26.2–27.8)	29.9 (29.1–30.8)	$p < 0.001$
BMI at 18 months [mean (95% CI)]	26.7 (25.9–27.5)	30.9 (30.0–31.8)	$p < 0.001$
BMI at 24 months [mean (95% CI)]	26.4 (25.6–27.2)	31.5 (30.6–32.4)	$p < 0.001$
% of initial weight lost at 2 years [mean (95% CI)]	21.6 (19.3–23.9)	5.5 (3.2–7.9)	
% excess weight lost at 12 months [mean (95% CI)]	78.6 (69.2–88.1)	41.1 (31.2–50.9)	$p < 0.001$
% excess weight lost at 2 years [mean (95% CI)]	87.2 (77.7–96.6)	21.8 (11.9–31.6)	$p < 0.001$
Proportion achieving excess weight loss > 50% at 2 years	33/39 (85%)	8/31 (26%)	$p < 0.001$
Proportion achieving satisfactory weight loss (> 25% excess weight lost)	39/40 (98%)	14/40 (35%)	$p < 0.001$
Mingrone, 2002[119]	**BPD (n = 46)**	**Diet (n = 33)**	
Weight (kg) women			
Baseline	125.3 (± 12.8)	121.6 (± 24.1)	
1 year, p-value vs baseline	90.2 (± 15.0), $p < 0.0001$	114.5 (± 24.5)	
Weight (kg) men			
Baseline	151.8 (± 17.1)	147.3 (± 26.8)	
1 year, p-value vs baseline	99.7 (± 7.0), $p < 0.0001$	138.2 (± 27.1)	
BMI women			
Baseline	48.3 (± 6.3)	48.4 (± 8.9)	
1 year, p-value vs baseline	35.2 (± 7.6), $p < 0.0001$	43.8 (± 7.7)	
BMI men			
Baseline	48.0 (± 5.4)	47.8 (± 8.8)	
1 year, p-value vs baseline	30.4 (± 3.5), $p < 0.0001$	44.8 (± 8.4)	
Fat-free mass (kg) women			
Baseline	59.3 (± 5.6)	58.3 (± 8.8)	
1 year, p-value vs baseline	50.5 (± 4.7), $p < 0.0001$	56.7 (± 8.8)	

TABLE 17 *Summary of results: surgery versus non-surgical management – weight change (continued)*

Fat-free mass (kg) men

Baseline	88.7 ($\pm$ 8.1)	87.3 ($\pm$ 11.4)
1 year, *p*-value vs baseline	74.2 ($\pm$ 5.4), $p < 0.0001$	83.7 ($\pm$ 11.8)

Fat mass (kg) women

Baseline	65.9 ($\pm$ 10.2)	63.3 ($\pm$ 16.2)
1 year, *p*-value vs baseline	39.8 ($\pm$ 12.7), $p < 0.0001$	57.8 ($\pm$ 16.5)

Fat mass (kg) men

Baseline	63.1 ($\pm$ 10.2)	60.0 ($\pm$ 15.6)
1 year, *p*-value vs baseline	25.5 ($\pm$ 2.7), $p < 0.0001$	54.6 ($\pm$ 15.6)

SOS study, 1997–2007[97,99,100]	**Surgery**	**Control**	
% weight change at 2 years[97]	-23.4 (*n* = 1845)	0.1 (*n* = 1660)	Difference 22.2 (21.6 to 22.8), $p < 0.001$
% BMI change at 2 years[97]	-23.3 (*n* = 1845)	0.1 (*n* = 1845)	22.1 (21.5 to 22.7), $p < 0.001$
Weight at 10 years, kg[100]	100.5 ($\pm$ 17.7) (*n* = 655)	115.2 ($\pm$ 19.9) (*n* = 621)	$p < 0.0001$
Weight change at 10 years (kg)[100]	-19.7 ($\pm$ 15.8) (*n* = 655)	1.3 ($\pm$ 13.8) (*n* = 621)	$p < 0.0001$
Weight % change at 10 years[100]	-16 ($\pm$ 12.1) (*n* = 655)	1.5 ($\pm$ 9.9) (*n* = 621)	
BMI at 10 years[100]	35.3 ($\pm$ 5.4) (*n* = 655)	40.6 ($\pm$ 5.9) (*n* = 621)	
Change in BMI at 10 years[100]	-6.7 ($\pm$ 5.4) (*n* = 655)	0.7 ($\pm$ 4.9) (*n* = 621)	$p < 0.0001$

Buddeberg-Fischer, 2006[105]	**Surgery (n = 63)**	**No surgery (n = 30)**	
BMI at mean 3.2 years	34.9 ($\pm$ 5.5)	40.6 ($\pm$ 7.4)	$p < 0.09$
BMI change at mean 3.2 years	-21.0 ($\pm$ 13.4)	-5.5 ($\pm$ 11.1)	$p < 0.001$
% EWL at mean 3.2 years	42.2 ($\pm$ 23.4)	11.5 ($\pm$ 25.8)	$p < 0.001$

Stoeckli, 2004[102–104]	**LAGB (n = 8)**	**Open RYGBP (n = 5)**	**Controls (n = 7)**	
BMI				
Baseline	41.7 ($\pm$ 2.8)	43.6 ($\pm$ 4.4)	41.1 ($\pm$ 2.6)	
24 months	33.2 ($\pm$ 4.7)*	32.9 ($\pm$ 6.7)*	41.0 ($\pm$ 3.4)	* vs control $p < 0.001$
Weight, mean (SEM) kg				
Baseline	117.2 (2.5)	113.3 (4.9)	113.5 (4.9)	
% change	-16.0 (3.2) $p < 0.01$	-28.6 (3.6)	$+0.5$ (1.2)	
Total fat mass, mean (SEM) kg				
Baseline	63.7 (2.2)	63.6 (2.2)	64.8 (4.7)	
% change	-33.9 (5.3) $p < 0.001$	-51.0 (5.2)	$+2.5$ (3.3)	

BMI, body mass index; BPD, biliopancreatic diversion; CI, confidence interval; Con therapy, conventional therapy; EWL, exccess weight loss; LAGB, laparoscopic adjustable gastric banding; LRYGBP, laparoscopic Roux-en-Y gastric bypass; open, open surgery; RYGBP, Roux-en-Y gastric bypass; SD, standard deviation; SEM, standard error of the mean; SOS, Swedish Obese Subjects.

All mean ($\pm$ SD) unless stated.

Quality of life was not reported by either Dixon and colleagues[117] or Mingrone and colleagues.[119]

Cohort studies

The SOS study assessed Health Related Quality of Life (HRQoL) using several measures, including general health perceptions from the General Health Rating Index, social interaction from the Sickness Impact Profile, overall mood from the Mood Adjective Check List (MACL), the obesity-related problems scale and the Hospital Anxiety and Depression scale. At baseline the patients in the surgery group had generally worse HRQoL than those in the conventional treatment group.[86,100] These differences may reflect the significant differences in BMI and prevalence of hypertension that developed between matching of controls and start of treatment, or may indicate bias in the selection of patients for surgery.

The two-year results of 974 participants have been tabulated and discussed in the previous report[15] and can be seen in Appendix 5. In brief, at two years follow-up gastric surgery patients had significant improvements in all HRQoL measures compared with patients receiving conventional treatment. These changes were significantly related to the magnitude of the weight loss and may have been expected given that the patients in the surgical group had significantly higher BMI at the time of treatment compared with the controls.[86]

A more recent report of 1276 participants found that improvements in HRQoL, which peaked one year after surgery, were followed by a gradual decline between one and six years, and then observations were relatively stable between six and ten years follow-up.[100] All HRQoL measures were improved at 10 years compared with baseline for the surgery group, but for the conventional group some had improved while others had worsened. After 10 years follow-up, the mean level of current health perception, social interaction, obesity-related problems, overall mood and depression did not differ significantly between the surgery and conventional treatment groups, although the surgery group had more anxiety ($p < 0.01$). However, statistically significantly greater 10-year change was observed in the surgery group for current health perceptions, social interaction, obesity-related problems and depression. There was no statistically significant difference in 10-year change for overall mood and anxiety (*Table 18*).

Buddeberg-Fischer and colleagues[105] applied a range of validated questionnaires related to quality of life to participants via telephone interview. The study reported that the Psychosocial Stress and Symptom Questionnaire (PSSQ) was used which incorporated the Hospital Anxiety and Depression Scale (HADS), the Bing Scale Questionnaire (BSQ) and the Psychosocial Assessment Questionnaire (PAssQ), although no results were reported for the overall PSSQ questionnaire. After a mean follow-up of 3.2 years there were no statistically significant differences between groups on mean scores from any of the three questionnaires (*Table 18*).

Buddeberg-Fischer and colleagues[105] also presented self-reported assessment of overall physical and mental health. This was also undertaken via telephone interview and while the results give an indication of the individuals' perception of their health this was not a validated measure and is likely to be measuring the state of the individual at that particular point in time only. Higher proportions of participants in the surgical group (79.3%) rated their physical health as good compared with the no-surgery group (64.5%), but this was not statistically significantly different ($p = 0.10$). A similar pattern emerged for ratings of mental health (77.6% versus 67.7% for the two groups respectively, $p = 0.22$). No analysis was presented of the proportions rating their health as poor (Appendix 5).

Quality of life was not reported by Stoeckli and colleagues.[102–104]

Comorbidities

Randomised controlled trials

Dixon and colleagues assessed the effects of laparoscopic adjustable gastric banding compared with conventional therapy on measures of glycaemic control and use of diabetes medication among 60 obese people with Type 2 diabetes.[117] Remission of Type 2 diabetes at two years follow-up was statistically significantly ($p < 0.001$) higher following laparoscopic adjustable gastric banding (73%) than conventional therapy (13%) (RR 5.5; 95% CI 2.2, 14.00) (*Table 19*). Similarly, people undergoing laparoscopic adjustable gastric banding were statistically significantly less likely to suffer from metabolic syndrome (70% versus 13%, $p < 0.001$). Measures of glycaemic control improved more following laparoscopic adjustable gastric banding than conventional therapy with statistically significantly greater decreases in mean levels of HbA_{1c} (glycosylated haemoglobin; difference -1.43, 95% CI -2.1 to 0.80, $p < 0.001$), plasma glucose (difference -31.8, 95% CI -53.1 to -12.3, $p = 0.002$), plasma insulin (difference

TABLE 18 *Summary of results: surgery versus non-surgical management – quality of life*

O'Brien, 2006[115,116]	LAGB (n = 39)	Non-surgical (n = 33)	Effect size/p-value
Mean SF-36 domain scores,[a] at 2 years			
Physical function	90	87	$p < 0.05$
Physical role	92	70	$p < 0.05$
Pain	83	78	$p = ns$
General health	73	68	$p < 0.05$
Vitality	66	57	$p < 0.05$
Social functioning	85	81	$p = ns$
Emotional role	92	72	$p < 0.05$
Mental health	76	72	$p = ns$
SOS study, 1997–2007[100] [b]	**Surgery (n = 655)**	**Control (n = 621)**	
Current health perception[c]			
1-year follow-up,% improvement	48%	7%	
10-year follow-up	57.5 (± 26.8)	55.4 (± 25.1)	$p = ns$
10-year change	5.8 (± 27.6) (11% improvement)	−3.4 (± 25.2)	$p < 0.0001$
Effect size of change	0.21	−0.13	
Obesity-related problems[d]			
1-year follow-up,% improvement	~63%	7%	
10-year follow-up	29.7 (± 27.3)	31.3 (± 25.5)	$p = ns$
10-year change	28.3 (± 28.3)	9.6 (± 22.6)	$p < 0.0001$
Effect size of change	1.00	0.42	
Social interaction[e]			
1-year follow-up,% improvement	~60%	7%	
10-year follow-up	8.4 (± 12.4)	7.7 (± 11.1)	$p = ns$
10-year change	−3.2 (± 13.0)	0.5 (± 10.0)	$p < 0.01$
Effect size of change	0.25	−0.05	
MACL Overall mood[f]			
10-year follow-up	3.06 (± 0.59)	3.11 (± 0.56)	$p = ns$
10-year change	0.14 (± 0.56)	0.05 (± 0.51)	$p = ns$
Effect size of change	0.25	0.10	
HADS Depression[g]			
10-year follow-up	3.7 (± 3.7)	3.7 (± 3.5)	$p = ns$
10-year change	−1.4 (± 3.9)	−0.5 (± 3.4)	$p < 0.05$
Effect size of change	0.35	0.14	
HADS Anxiety[g]			
10-year follow-up	4.6 (± 4.4)	4.0 (± 4.2)	$p < 0.01$
10-year change	−1.4 (± 4.3)	−1.4 (± 3.9)	$p = ns$
Effect size of change	0.33	0.35	

TABLE 18 *Summary of results: surgery versus non-surgical management – quality of life (continued)*

Buddeberg-Fischer, 2006[105]	Surgery (n = 63)	No surgery (n = 30)	
HADS – Anxiety Score[g]: mean 3.2 years follow-up	5.76 (± 4.27)	6.53 (± 4.29)	$p = 0.21$
HADS – Depression Score[g]: mean 3.2 years follow-up	4.67 (± 4.58)	4.33 (± 3.01)	$p = 0.65$
BSQ Score[h]: mean 3.2 years follow-up	7.16 (± 9.68)	8.87 (± 9.52)	$p = 0.55$
PassQ Score[i]: mean 3.2 years follow-up	2.11 (± 2.04)	1.87 (± 2.08)	$p = 0.99$

BSQ, Bing Scale Questionnaire; HADS, Hospital Anxiety and Depression Scale; HRQol, health-related quality of life; LAGB, laparoscopic adjustable gastric banding; MACL, Mood Adjective Check List; ns, not statistically significant; PassQ, Psychosocial Assessment Questionnaire; SD, standard deviation; SF-36, short form health survey; SOS, Swedish Obese Subjects.

All mean (± SD) unless stated.

a Mean Short Form-36 QoL domain scores estimated from figure (95% CIs presented in figure but not possible to extract data reliably). Higher scores indicate better health status.
b SOS study: HRQoL at 10 years in surgically treated patients by weight change, and 10-year trends in weight loss and HRQoL in surgically treated patients with weight loss ≥ 10% vs < 10% after 10 years reported but not extracted. Effect size (ES) of change calculated to provide standardized effect levels regardless of sample size and scaling properties of HRQoL instruments (where 0 to < 0.20 trivial, 0.20 to < 0.50 small, 0.50 to < 0.80 moderate, ≥ 0.80 large).
c Health perceptions from the General Health Rating Index (score range 0–100, higher score indicates more positive perceived health status).
d Obesity-related problems scale (score range 0–100, higher score indicates greater impairment of psychosocial functioning).
e Social interaction from the Sickness Impact Profile (score range 0–100, higher score indicates more dysfunction in social interaction).
f Overall mood from the Mood Adjective Check List (a higher overall mood score indicates more positive mood states).
g Hospital Anxiety and Depression scale (a score of less than eight is considered in the normal range, a score of 8–10 indicates a possible case and a score > 10 indicates a probable case of mood disorder).
h Binge scale questionnaire (higher score indicates greater severity of binge eating).
i Psychosocial assessment questionnaire (score range 0–11, higher score indicates greater psychosocial stress).

– 13.4, 95% CI – 19.6 to – 7.3, $p < 0.001$), and HDL-cholesterol (difference 10.0, 95% CI 5.8 to 14.2, $p < 0.001$). There were greater improvements in other indices of glycaemic control (e.g. blood pressure, total cholesterol) for the laparoscopic adjustable gastric banding group compared with the conventional therapy group, although these were not statistically significant (Appendix 5). The benefits of laparoscopic adjustable gastric banding compared with conventional therapy were evident in the reduction in the use of diabetes medication. At two years follow-up a greater proportion of those receiving laparoscopic adjustable gastric banding no longer required diabetes medication compared with conventional therapy (change from baseline 83% versus 15% respectively, not tested for statistical significance). There were similar improvements from baseline to two years follow-up for those in the laparoscopic adjustable gastric banding group compared to the conventional therapy group in their use of metformin (86.3% versus 30.8%), other hypoglycaemics (27.6% versus 3.2%), insulin (3.4% versus 11.5%), anti-hypertensives (48% versus 0%) and lipid-lowering agents (27.6% versus 3.9%) although these

differences between the groups were also not tested for statistical significance.

O'Brien and colleagues noted that the group receiving laparoscopic adjustable gastric banding experienced a statistically significant reduction in the proportion of people with metabolic syndrome at two years follow-up (baseline 37.5%, two years 2.7%, $p < 0.001$).[115,116] For those in the non-surgical group the proportion with metabolic syndrome decreased, but not significantly (baseline 37.5%, two years 24%, $p = 0.22$). There was a statistically significant difference in the number of participants with metabolic syndrome between the two interventions, at two years $p = 0.006$ (*Table 19*).

Comorbidities were not reported by Mingrone and colleagues.[119]

Cohort studies
Earlier publications from the SOS study of two-year and eight-year data on the incidence of diabetes and hypertension in 483 participants[89] and two-year data on lipid disturbances in 1449 participants[88] have been summarised previously[15]

and can be seen in Appendix 5. More recently reported data including 3505 participants at two-year follow-up and 1268 participants at 10-year follow-up[97] are discussed here.

The incidence of diabetes (2 years: 1% versus 8%, $p < 0.001$; 10 years: 7% versus 24%, $p < 0.001$), hypertriglyceridaemia (2 years: 8% versus 22%, $p < 0.001$; 10 years: 17% versus 27%, $p = 0.03$) and hyperuricaemia (2 years: 4% versus 16%, $p < 0.001$; 10 years: 17% versus 28%, $p < 0.001$) was significantly lower in the surgery group at both 2 and 10 years follow-up (*Table 19*). The incidence of low HDL-cholesterol was significantly lower in the surgery group at two years (2% versus 10%, $p < 0.001$), but not 10 years (3% versus 6%, $p = 0.12$) follow-up, and there was no statistically significant difference in the incidence of hypertension (2 years: 24% versus 29%, $p = 0.06$; 10 years: 41% versus 49%, $p = 0.13$) and hypercholesterolaemia (2 years: 27% versus 24%, $p = 0.11$; 10 years: 30% versus 27%, $p = 0.57$) at 2 or 10 years follow-up. Participants who underwent surgery were more likely to recover from diabetes (2 years: 72% recovered versus 21%, $p < 0.001$; 10 years: 36% versus 13%, $p < 0.001$), hypertension (2 years: 34% recovered versus 21%, $p < 0.001$; 10 years: 19% versus 11%, $p = 0.02$), hypertriglyceridaemia (2 years: 62% recovered versus 22%, $p < 0.001$; 10 years: 46% versus 24%, $p < 0.001$), low HDL-cholesterol (2 years: 76% recovered versus 39%, $p < 0.001$; 10 years: 73% versus 53%, $p < 0.001$) and hyperuricaemia (2 years: 71% recovered versus 31%, $p < 0.001$; 10 years: 48% versus 27%, $p < 0.001$) than those with conventional treatment, at 2 and 10 years follow-up, but there was no statistically significant difference in recovery from hypercholesterolaemia between groups (2 years: 22% recovered versus 17%, $p = 0.07$; 10 years: 21% versus 17%, $p = 0.14$) (*Table 19*).

Of patients who were on diabetes medication at baseline, significantly fewer surgery patients were on diabetes medication at six years follow-up compared with controls [68.8% versus 100%, RR 0.71 (95% CI 0.56 to 0.89), $p < 0.05$]. This was also the case for patients who were not on diabetes medication at baseline [2.1% versus 11.3%, RR 0.20 (95% CI 0.10 to 0.38), $p < 0.05$].[136]

Of patients who were on CVD medication at baseline, significantly fewer surgery patients were on CVD medication at six years follow-up compared with controls [64.7% versus 86.4%, RR 0.77 (95% CI 0.67 to 0.88), $p < 0.05$]. Of patients who were not on medication at baseline, the difference in the proportion on medication

was statistically significant at two years follow-up [surgery 3.1%, control 10.1%, RR 0.28 (95% CI 0.14 to 0.56), $p < 0.05$], but not at six years follow-up [surgery 13.3%, control 16.7%, RR 0.80 (95% CI 0.56 to 1.16)].[136]

At two years follow-up, men with surgery had more cholelithiasis [4.0% versus 1.2%, $p = 0.011$, OR 4.2 (95% CI 1.5 to 12.0)], cholecystectomy [3.4% versus 0.7%, $p = 0.008$, OR 5.4 (95% CI 1.5 to 19.6], cholecystitis [2.5% versus 0.7%, $p = 0.058$, OR 4.5 (95% CI 1.2 to 17.1)] and total biliary disease [4.1% versus 1.5%, $p = 0.024$, OR 3.5 (95% CI 1.3 to 9.2)] than male controls. There was no difference in pancreatitis among men, and there were no statistically significant differences in these diseases among women.[96]

Incidence of cancer during an average of 11 years follow-up in the SOS study has been reported in a recent abstract.[101] In the surgery group ($n = 2010$) there were 126 cases of first-time cancers and in the control group ($n = 2037$) there were 173 cases. The unadjusted hazard ratio for overall cancer incidence was 0.71 ($p = 0.003$) and the hazard ratio adjusted for risk factors was 0.74 ($p = 0.011$). The unadjusted hazard ratio for men ($n = 1178$) was 0.98 (95% CI 0.63–1.51, $p = 0.91$) and for women ($n = 2867$) was 0.63 (95% CI 0.48–0.82, $p = 0.001$) (Appendix 5).

Only data on medication use were reported by Buddeberg-Fischer and colleagues.[105] In the last three months of the study those in the surgery group were found to use statistically significantly fewer numbers of different obesity-related drugs than those in the no-surgery group ($p < 0.001$). There were no statistically significant differences in the number of different medications being taken for somatic comorbidity or psychiatric comorbidity (*Table 19*). Caution is required in interpreting these outcomes as these were medications used only in the last three months of a study with a mean of 3.2 years follow-up, no measures of variance around the mean values were reported, results were based on self-reports and no further definition of the drugs was given.

Comorbidities were not reported by Stoeckli and colleagues.[102–104]

Complications and additional operative procedures
Randomised controlled trials
O'Brien and colleagues found a higher proportion of adverse events among those people in the non-surgical therapy group (58%, $n = 31$) than

TABLE 19 *Summary of results: surgery versus non-surgical management – comorbidities*

Dixon, 2008[117]	*LAGB* *(n = 30)*	*Con therapy* *(n = 30)*	*Effect size/p-value* *(95% CI)*
Remission of Type 2 diabetes at 2 years	22/30 (73%)	4/30 (13%)	RR 5.5 (95% CI 2.2 to 14.0) $p < 0.001$
Metabolic syndrome[a]			
At baseline	1 (3%)	1 (3%)	
At 2 years	21 (70%); $p < 0.001$	4 (13%); $p = 0.22$	$p < 0.001$
No diabetes medication			
At baseline	2/29 (6.9%)	4/26 (15.4%)	
At 2 years	26/29 (89.7%)	8/26 (30.8%)	
Metformin use			
At baseline	28/29 (96.6%)	26/26 (100%)	
At 2 years	3/29 (10.3%)	18/26 (69.2%)	
Other hypoglycaemic use			
At baseline	9/29 (31%)	8/26 (30.8%)	
At 2 years	1/29 (3.4%)	7/26 (26.9%)	
Insulin use			
At baseline	1/29 (3.4%)	0	
At 2 years	0	3/26 (11.5%)	
Antihypertensive agents			
At baseline	20/29 (70%)	15/26 (57.7%)	
At 2 years	6/29 (20.7%)	15/26 (57.7%)	
Lipid-lowering agents			
At baseline	12/29 (41.4%)	8/26 (30.8%)	
At 2 years	4/29 (13.8%)	7/26 (26.9%)	
O'Brien, 2006[115,116]	*LAGB (n = 39)*	*Non-surgical* *(n = 33)*	
Metabolic syndrome			
Before treatment	15/40 (37.5%)	15/40 (37.5%)	
2 years after treatment	1/39 (2.7%)	8/33 (24%)	$p = 0.006$
SOS study, 1997–2007[96,97,136,b]	*Surgery*	*Controls*	
Incidence of diabetes at 2 years	15/1489 (1%)	112/1402 (8%)	OR 0.14 (0.08 to 0.24), $p < 0.001$
Incidence of diabetes at 10 years	36/517 (7%)	129/539 (24%)	OR 0.25 (0.17 to 0.38), $p < 0.001$
Recovery of diabetes at 2 years	246/342 (72%)	52/248 (21%)	OR 8.42 (5.68 to 12.5), $p < 0.001$
Recovery of diabetes at 10 years	42/118 (36%)	11/84 (13%)	3.45 (1.64 to 7.28), $p < 0.001$
No. on diabetes medication[136] at baseline	$(n=32)$	$(n=21)$	
% at 2 years	56.2	100.0	RR 0.56 (0.41 to 0.76), $p < 0.05$
% at 6 years	68.8	100.0	RR 0.71 (0.56 to 0.89), $p < 0.05$
No. not on diabetes medication[136] at baseline	$(n=478)$	$(n=434)$	
% at 2 years	0.2	3.7	RR 0.08 (0.01 to 0.58), $p < 0.05$

TABLE 19 *Summary of results: surgery versus non-surgical management – comorbidities (continued)*

% at 6 years	2.1	11.3	RR 0.20 (0.10 to 0.38), $p < 0.05$
Incidence of hypertension at 2 years	149/623 (24%)	223/770 (29%)	OR 0.78 (0.60 to 1.01), $p = 0.06$
Incidence of hypertension at 10 years	88/215 (41%)	137/279 (49%)	OR 0.75 (0.52 to 1.08), $p = 0.13$
Recovery from hypertension at 2 years	409/1204 (34%)	185/880 (21%)	1.72 (1.40 to 2.12), $p < 0.001$
Recovery from hypertension at 10 years	81/424 (19%)	38/342 (11%)	OR 1.68 (1.09 to 2.58), $p = 0.02$
Incidence of hypertriglyceridaemia at 2 years	58/731 (8%)	176/801 (22%)	OR 0.29 (0.21 to 0.41), $p < 0.001$
Incidence of hypertriglyceridaemia at 10 years	38/225 (17%)	75/281 (27%)	OR 0.61 (0.39 to 0.95), $p = 0.03$
Recovery from hypertriglyceridaemia at 2 years	683/1102 (62%)	187/850 (22%)	OR 5.28 (4.29 to 6.49), $p < 0.001$
Recovery from hypertriglyceridaemia at 10 years	185/402 (46%)	79/331 (24%)	OR 2.57 (1.85 to 3.57), $p < 0.001$
Incidence of low HDL-cholesterol at 2 years	25/1293 (2%)	117/1174 (10%)	OR 0.21 (0.14 to 0.32), $p < 0.001$
Incidence of low HDL-cholesterol at 10 years	13/431 (3%)	26/440 (6%)	OR 0.57 (0.29 to 1.15), $p = 0.12$
Recovery from low HDL-cholesterol at 2 years	338/445 (76%)	154/396 (39%)	5.28 (3.85 to 7.23), $p < 0.001$
Recovery from low HDL-cholesterol at 10 years	123/169 (73%)	88/166 (53%)	2.35 (1.44 to 3.84), $p < 0.001$
Incidence of hypercholesterolaemia at 2 years	136/504 (27%)	143/596 (24%)	OR 1.27 (0.95 to 1.69), $p = 0.11$
Incidence of hypercholesterolaemia at 10 years	40/135 (30%)	51/188 (27%)	OR 1.16 (0.69 to 1.95), $p = 0.57$
Recovery from hypercholesterolaemia at 2 years	292/1327 (22%)	178/1048 (17%)	1.22 (0.98 to 1.51), $p = 0.07$
Recovery from hypercholesterolaemia at 10 years	105/498 (21%)	74/435 (17%)	OR 1.30 (0.92 to 1.83), $p = 0.14$
Incidence of hyperuricaemia at 2 years	42/1044 (4%)	163/1017 (16%)	OR 0.22 (0.15 to 0.31), $p < 0.001$
Incidence of hyperuricaemia at 10 years	58/342 (17%)	107/382 (28%)	OR 0.49 (0.34 to 0.71), $p < 0.001$
Recovery from hyperuricaemia at 2 years	562/792 (71%)	197/637 (31%)	OR 5.36 (4.23 to 6.78), $p < 0.001$
Recovery from hyperuricaemia at 10 years	140/292 (48%)	66/243 (27%)	OR 2.37 (1.61 to 3.47), $p < 0.001$
Biliary disease and pancreatitis frequencies over 2 years (%)[96]			
	(n = 1422)	(n = 1260)	
Cholelithiasis			
Men	4.0	1.2	OR 4.2 (1.5 to 12.0), $p = 0.011$
Women	5.5	4.5	OR 1.1 (0.7 to 1.8), $p = 0.328$
Cholecystitis			
Men	2.5	0.7	OR 4.5 (1.2 to 17.1), $p = 0.058$
Women	3.3	2.5	OR 1.4 (0.7 to 2.5), $p = 0.379$
Cholecystectomy			
Men	3.4	0.7	OR 5.4 (1.5 to 19.6), $p = 0.008$
Women	3.5	2.3	OR 1.6 (0.9 to 3.0), $p = 0.191$

TABLE 19 *Summary of results: surgery versus non-surgical management – comorbidities (continued)*

Total biliary disease			
Men	4.1	1.5	OR 3.5 (1.3 to 9.2), $p = 0.024$
Women	6.8	5.3	OR 1.2 (0.8 to 1.9), $p = 0.223$
Pancreatitis			
Men	1.1	0.2	OR 3.6 (0.4 to 31.2), $p = 0.219$
Women	0.7	0.4	OR 1.8 (0.4 to 7.6) $p = 0.514$
Cardiovascular disease medication[136]			
On medication at baseline	$n = 150$	$n = 125$	
% on medication at 2 years	61.7	91.2	RR 0.69 (0.60 to 0.80), $p < 0.05$
% on medication at 6 years	64.7	86.4	RR 0.77 (0.67 to 0.88), $p < 0.05$
Not on medication at baseline	$n = 360$	$n = 330$	
% on medication at 2 years	3.1	10.1	RR 0.28 (0.14 to 0.56), $p < 0.05$
% on medication at 6 years	13.3	16.7	RR 0.80 (0.56 to 1.16)
***Buddeberg-Fischer, 2006*[105]**	***Surgery*** ***(n = 59/63)***	***No surgery*** ***(n = 30/30)***	
Number of different drugs at mean 3.2 years for [mean, median (range)]:			
Obesity	0.03, 0 (0–1)	0.32, 0 (0–2)	$p < 0.001$
Somatic comorbidity	2.29, 2 (0–15)	2.10, 1 (0–9)	$p = 0.98$
Psychiatric comorbidity	0.17, 0 (0–3)	0.6, 0 (0–2)	$p = 0.25$

CI, confidence interval; Con therapy, conventional therapy; LAGB, laparoscopic adjustable gastric banding; OR, odds ratio; RR, relative risk; SOS, Swedish Obese Subjects.
All mean ($\pm$ SD) unless stated.
a   Reports the number of patients not meeting the criteria for metabolic syndrome.
b   For incidence of and recovery from comorbidities at 2 and 10 years the n values used for numerators were calculated by reviewer and rounded.

in the laparoscopic adjustable gastric banding group (18%, $n = 39$)[115,116] (*Table 20*). For those receiving non-surgical therapy the most common adverse events were intolerance to orlistat (26%), acute cholecystitis (13%), the need for operative interventions (13%) and intolerance to a VLCD (3%). Adverse events reported by people in the laparoscopic adjustable gastric banding group included operative interventions (13%), laparoscopic revision (prolapse or posterior) (10%), 5-mm port site infection (2.6%) and acute cholecystitis (2.6%). Loss to follow-up was higher in the non-surgical group (16%) compared with the laparoscopic adjustable gastric banding group (2.6%) (but reasons were not given).

Dixon and colleagues reported several adverse events among people in the laparoscopic adjustable gastric banding group ($n = 30$), including a superficial wound infection (one patient), gastric pouch enlargement requiring revisional surgery

(two patients), eating difficulties and persistent regurgitation requiring band removal (one patient), postoperative febrile episode (one patient), hypoglycaemic episode (one patient) and gastrointestinal tract intolerance to metformin (one patient)[117] (*Table 20*). People in the conventional therapy group ($n = 30$) suffered minor adverse events associated with their medication which resolved following discontinuation of treatment, including gastrointestinal problems (two patients), persistent diarrhoea with metformin (one patient), and vasculitic rash (one patient). Other adverse events included multiple hypoglycaemic episodes (one patient), angina and transient cerebral ischaemic episode requiring admission to hospital (one patient) and intolerance to very-low-calorie meal replacement (two patients). Dixon and colleagues noted that the mean procedure time for placement of the laparoscopic adjustable gastric banding was 54 minutes and that 80% of patients were kept in hospital for only one day.

Complications and additional operative procedures were not reported by Mingrone and colleagues.[119]

Cohort studies
Within 90 days of surgery in the SOS study there were five deaths (0.25%) in the surgery group (four from peritonitis with organ failure, one from sudden death) and two deaths in the control group (one from pancreatic cancer, one from alcohol-related causes).[99]

Perioperative complications were experienced by 13% of 1164 patients in the SOS study, these included bleeding (0.9%), thromboembolic events (0.8%), wound complications (1.8%), abdominal infection (2.1%), pulmonary symptoms (6.2%) and miscellaneous (4.8%) (*Table 20*). Postoperative complications requiring reoperation were experienced by 2.2% of patients in the surgery group. The patients in the SOS study underwent vertical banded gastroplasty, gastric banding or gastric bypass, but the complications are only reported for the surgery group as a whole. Surgical reoperations or conversions (excluding operations caused by postoperative complications) were reported for 1338 patients followed for at least 10 years, and occurred in 31% of gastric banding patients, 21% of vertical banded gastroplasty patients and 17% of gastric bypass patients.

The Buddeberg-Fischer and colleagues[105]cohort study reported reoperations only. Seven of 69 participants in the surgery group were reported to have a reoperation; five participants with laparoscopic gastric banding were converted to Roux-en-Y gastric bypass and two had their bands removed. Nine patients in the no-surgery group underwent gastric bypass. No further details are reported.

Complications and additional operative procedures were not reported by Stoeckli and colleagues.[102–104]

Cumulative overall mortality
The SOS study reported cumulative overall mortality during a period of up to 16 years (mean 10.9 years follow-up).[99] The hazard ratio of the surgery group compared with the control group was 0.76 [(95% CI 0.59 to 0.99) $p = 0.04$]. There were 101 (5%) deaths in the surgery group and 129 deaths (6.3%) in the control group. *Table 21* displays the causes of death; the most common

causes of death were cancer (surgery 29 cases, control 47 cases), sudden death (surgery 20 cases, control 14 cases) and myocardial infarction (surgery 13 cases, control 25 cases).

Summary
Three RCTs (one with a low risk of selection bias, one with a high risk of selection bias and one of uncertain risk of bias) and three cohort studies (of variable size and quality) were included. Regardless of the surgical intervention used or the type of patients included, all studies reporting a statistical comparison found statistically significant benefits on measures of weight change compared with no surgery at two to three years follow-up. A large cohort study found weight loss was still significantly greater at 10 years follow-up compared with conventional treatment. One RCT found statistically significantly greater improvements in five of eight domains of the SF-36 following laparoscopic adjustable gastric banding compared with no surgery, but one cohort study found no statistically significant difference in mean scores of the PSSQ between surgery and no-surgery groups. The SOS study found mixed results in HRQoL at 10 years follow-up, with significantly greater 10-year change following surgery observed in some measures, but not others. The RCT of people with Type 2 diabetes found significantly higher remission of the disease following laparoscopic adjustable gastric banding than conventional therapy, and two RCTs reporting metabolic syndrome found significantly fewer people with the syndrome two years after surgery. The SOS study found a statistically significant reduction in the incidence in three of six comorbidities assessed at 10-year follow-up after surgery compared with conventional therapy. Significantly fewer surgery patients than conventional therapy patients were on diabetes medication at two and six years follow-up, and on CVD medication at two, but not six years follow-up. Two RCTs reported adverse events from following surgery (e.g. operative interventions, revisional surgery, port-site infection) and from conventional therapy (e.g. intolerance to medication, acute cholecystitis, need for operative intervention, gastrointestinal problems). Within 90 days of surgery in the SOS study there were five deaths (0.25%) in the surgery group and two deaths in the control group. Perioperative complications occurred in 13% of patients.

TABLE 20 *Summary of results: surgery versus non-surgical management – complications and additional procedures*

Dixon, 2008[117]	*LAGB (n = 30)*	*Conventional therapy (n = 30)*
Mean procedure time (SD, range)	54 minutes (10.8, 40 to 74)	
Length of hospital stay		
1 day	23 (80%)	
2 day	5 (17%)	
4 days	1 (3%)	
Adverse events (n)		
Superficial wound infection	1	
Gastric pouch enlargement at 10 months	2	
Band removal	1	
Febrile episodes	1	
Minor hypoglycaemic episode	1	
Intolerance to metformin	1	
Minor gastrointestinal tract adverse events		2
Persistent diarrhoea with metformin		1
Vasculitic rash		1
Multiple hypoglycaemic episodes		1
Angina and transient cerebral ischaemic episode		1
Intolerant to very low-calorie meal replacement		2
O'Brien, 2006[115,116]	*LAGB (n = 39)*	*Non-surgical (n = 31)*
Total of adverse events (%)	7/39 (18)	18/31 (58)
5-mm port site infection (%)	1/39 (2.6)	n/a
Acute cholecystitis (%)	1/39 (2.6)	4/31 (13)
Prolapse, posterior (laparoscopic revision) (%)	4/39 (10)	n/a
Intolerance to very-low-calorie diet (%)	n/a	1/31 (3)
Intolerance to orlistat (%)	n/a	8/31 (26)
Operative interventions (%)	5/39 (13)[a]	4/31 (13)[b]
SOS study, 1997–2007[99]	*Surgery (n = 2010)*	*Control (n = 2037)*
Deaths within 90 days of surgery	5 (0.25%) (four peritonitis with organ failure, one sudden death)	2 (0.10%) (one pancreatic cancer, one alcohol-related causes)
Peri/postoperative complications[97,137]	(n = 1164)	
No. of patients with complications (%)	151 (13%)	
Total no. of complications	193	
Bleeding	0.9%	
Thromboembolic events	0.8%	
Wound complications	1.8%	
Abdominal infection	2.1%	
Pulmonary symptoms	6.2%	
Miscellaneous	4.8%	

TABLE 20 *Summary of results: surgery versus non-surgical management – complications and additional procedures (continued)*

Postoperative complications requiring reoperation	26 patients (2.2%)	
Surgical reoperations or conversions (excluding operations caused by postoperative complications) in those followed up for at least 10 years	(*n* = 1338); banding 31%, VBG 21%, GBP 17%	
Buddeberg-Fischer, 2006[105]	**Surgery (*n* = 56)**	**No surgery (*n* = 37)**
Reoperation	7/56; LAGB (*n* = 47) conversion to RYGBP 5, reversed (debanding) 2; RYGBP (*n* = 9) 0	Underwent RYGBP 9/37

GBP, gastric bypass; LAGB, laparoscopic adjustable gastric banding; RYGBP, Roux-en-Y gastric bypass; SOS, Swedish Obese Subjects; VBG, vertical banded gastroplasty.
a The operative interventions were undertaken for the following adverse events: the four cases of prolapse of the posterior gastric wall through the band, and the single case of acute cholecystitis.
b The operative interventions were all undertaken for the adverse event of acute cholecystitis that occurred in four patients.

Comparisons of different surgical procedures
Gastric bypass versus vertical banded gastroplasty
Weight change

Three of the seven RCTs that compared vertical banded gastroplasty with gastric bypass (open or laparoscopic surgery) demonstrated statistically significantly greater percentage of excess weight loss with gastric bypass[108,109,120,123] (*Table 22*). Howard and colleagues[120] found that patients with open gastric bypass (*n* = 20) had 78% excess weight loss compared with 52% excess weight loss for patients undergoing open vertical banded gastroplasty (*n* = 22) (*p* < 0.05) at 12 months follow-up. At five years excess weight loss was 70% and 37% for gastric bypass and vertical banded gastroplasty, respectively (*p* < 0.05), although only six patients in each group were followed for this length of time. All gastric bypass patients had lost at least 50% of excess weight at 12 months and 60 months follow-up, whereas only 55% of vertical banded gastroplasty patients had achieved this at 12 months, and none by 60 months (*p*-value not stated, Appendix 6). Sugerman and colleagues[123] found that excess weight loss for open gastric bypass was significantly greater than for open vertical banded gastroplasty at 12 months [68%

TABLE 21 *Overall mortality from the SOS study*

SOS study[99]	Surgery (*n* = 2010)	Control (*n* = 2037)
Number of deaths (%)	101/2010 (5.0%)	129/2037 (6.3%)
Cause of death: cardiovascular condition		
Any event (number of subjects)	43	53
Cardiac[a]	35	44
Stroke	6	6
Other	2	3
Cause of death: non-cardiovascular		
Any event (number of subjects)	58	76
Tumour	29 (all cancer)	48 (47 cancer, 1 non-malignant)
Infection	12	3
Thromboembolic disease	5	7
Other	12	18

SOS, Swedish Obese Subjects.
a Cardiac events included myocardial infarction, heart failure and sudden death.

(SD 17) versus 43% (SD 18), $p < 0.001$], 24 months [66% (SD 29) versus 39% (SD 24), $p < 0.001$] and 36 months [62% (SD 18) versus 37% (SD 19), $p < 0.001$]. As previously stated, this study has a high risk of bias because recruitment was stopped early when a significant difference ($p < 0.05$) in weight loss was noted in favour of gastric bypass. At this point 20 patients had been recruited to each arm of the study, and were followed up for three years. Before surgery, Sugerman and colleagues classified patients as 'sweets eaters' or 'non-sweets eaters'. They noted that gastric bypass surgery led to a significantly greater excess weight loss for sweets eaters than did vertical banded gastroplasty ($p < 0.0001$). For non-sweets eaters gastric bypass caused greater decreases in excess weight compared with vertical banded gastroplasty, but differences were not significant [$p = $ ns (not statistically significant)] (Appendix 6). The authors attribute this difference to the development of dumping syndrome symptoms in sweets eaters with gastric bypass. However, caution is required when interpreting these results because sample sizes were small and the comparisons were not randomised. A third study, Olbers and colleagues,[108,109] which compared laparoscopic gastric bypass with laparoscopic vertical banded gastroplasty also reported that excess weight loss for gastric bypass was significantly greater than for vertical banded gastroplasty at 12 months [78.3% (SD 20) versus 62.9% (SD 28.4), $p = 0.009$], and at 24 months [84.4% (SD 22.1) versus 59.8% (SD 29.6), $p < 0.001$]. A greater proportion of patients (34 of 36) who received laparoscopic gastric bypass achieved an excess weight loss of at least 50% without remedial surgery, in comparison to those receiving laparoscopic vertical banded gastroplasty (21 of 35) (Appendix 6). Weight loss was also reflected in mean BMI values which had fallen to 29 in the laparoscopic Roux-en-Y gastric bypass group and 32 in the laparoscopic vertical banded gastroplasty group (*p*-value not reported), but there was little further change at two years when BMI values were 28 and 32, respectively (*p*-value not reported).

Two of the seven trials reported greater weight loss in the gastric bypass group, but did not indicate whether or not this difference was statistically significant (*Table 22*). The trial by Agren and Naslund,[73] which was reported only as an abstract, found greater mean excess weight loss with loop gastric bypass (76.6%) than with vertical banded gastroplasty (59.8%) at 18 months follow-up. Lee and colleagues[124] compared laparoscopic gastric bypass and laparoscopic vertical banded gastroplasty and reported that at two years follow-

up the gastric bypass group had lower BMI (28.5 versus 31.9) and greater excess weight loss (71.4% versus 53.1%).

The remaining two trials that compared gastric bypass with vertical banded gastroplasty found that there was no significant difference in weight loss between the groups (*Table 22*). VanWoert and colleagues[106] reported, in an abstract only, per cent of ideal body weight at 36 months to be 121% in the gastric bypass group, and 123% in the vertical banded gastroplasty group. Success rates, defined as a BMI < 35 or < 50% excess weight and reoperation not required, were compared for Roux-en-Y gastric bypass and vertical banded gastroplasty with surgical isolation of the gastric pouch by MacLean and colleagues.[121,122] When compared at three years and five to six years follow-up, there was no significant difference in success rates between gastric bypass and vertical banded gastroplasty [about three years: 58% versus 39% ($p = 0.08$); five to six years: 34% versus 16%, ($p = 0.112$)]. Failures were converted to isolated gastric bypass, which had a success rate of 63% at five to six years. Although comparisons of the three procedures were reported to show a significantly greater success rate for isolated gastric bypass compared with gastric bypass ($p < 0.0009$) and vertical banded gastroplasty ($p = 0.0001$), these were not valid because the periods of follow-up differed.

Quality of life and comorbidities
Only one RCT comparing gastric bypass with vertical banded gastroplasty reported on QoL measures, and this study performed both procedures laparoscopically.[124] Using the gastrointestinal quality of life index (GIQLI), patients in both groups had significant improvements in physical function, emotional function and social function domains, but patients with vertical banded gastroplasty had a significant decrease in the domain of symptoms (*p*-values not reported) (*Table 23*). Patients with gastric bypass scored significantly better on seven of 19 symptom items, four of five emotional items, one of seven physical items and two of five social items (*p*-values ranged from $p = 0.04$ to $p < 0.001$, see Appendix 6). Patients with vertical banded gastroplasty scored better on the symptom of abdominal flatulence ($p = 0.02$).

Data on comorbidities were not assessed.

Complications and additional operative procedures
Of the seven RCTs comparing vertical banded gastroplasty with gastric bypass surgery, five

TABLE 22 *Summary of results: gastric bypass versus vertical banded gastroplasty – weight change*

Howard, 1995[120]	GBP (n = 20)	VBG (n = 22)	p-value
% excess weight loss 1 year[a]	78 (n = 20)	52 (n = 20)	p < 0.05
% excess weight loss 5 years[a]	70 (n = 6)	37 (n = 6)	p < 0.05
Patients with at least 50% of excess weight loss			
12 months	100%	55%	p not stated
60 months	100% (n = 6)	0% (n = 6)	p not stated
Patients with more than 75% of excess weight loss			
12 months	60%	18%	p not stated
60 months	50% (n = 6)	0% (n = 6)	p not stated
Sugerman, 1987[123]	RYGBP (n = 20)	VBG (n = 20)	
% excess weight loss 1 year	68 (± 17) n = 19	43 (± 18) n = 18	p < 0.001
% excess weight loss 2 years[a]	66 (± 29) n = 18	39 (± 24) n = 17	p < 0.001
% excess weight loss 3 years[a]	62 (± 18) n = 18	37 (± 19) n = 16	p < 0.001
% ideal body weight 12 months	138 (± 32) n = 19	176 (± 41) n = 18	p < 0.01
% ideal body weight 24 months	139 (± 32) n = 18	178 (± 41) n = 17	p < 0.01
% ideal body weight 36 months	142 (± 37) n = 18	180 (± 44) n = 16	p < 0.01
Weight loss (kg) 12 months	43.5 (± 11.3) n = 19	32.2 (± 10.9) n = 18	p < 0.001
Weight loss (kg) 24 months	43.5 (± 15.4) n = 18	30.4 (± 12.2) n = 17	p < 0.001
Weight loss (kg) 36 months	41.3 (± 12.7) n = 18	27.2 (± 14.5)	p < 0.01
% weight lost 12 months	33 (± 7) n = 19	22 (± 8) n = 18	p < 0.001
% weight lost 24 months	33 (± 9) n = 18	22 (± 9) n = 17	p < 0.001
% weight lost 36 months	32 (± 9) n = 18	20 (± 10) n = 16	p < 0.01
Olbers, 2005[108,109]	LRYGBP (n = 37)	LVBG (n = 46)	
% excess weight loss 1 year	78.3 (± 20.0) n = 36	62.9 (± 28.4) n = 39	p = 0.009
% excess weight loss 2 years	84.4 (± 22.1) n = 36	59.8 (± 29.6) n = 35	p < 0.001
BMI at 1 year[a]	29 (n = 36)	32 (n = 39)	
BMI at 2 years[a]	28 (n = 36)	32 (n = 35)	
Proportion achieving excess weight loss of at least 50% without remedial surgery after 2 years	34/36 (94.4%)	21/35 (60%)	
Agren and Naslund, 1989[73]	Loop GBP (n = 25)	VBG (n = 27)	
% excess weight loss 1 year	76.6	58.3	
% excess weight loss 18 months	76.6	59.8	
Lee, 2004[124]	LRYGBP (n = 40)	LVBG (n = 40)	
% excess weight loss 1 year	62.9 (n = 40)	55.4 (n = 40)	
% excess weight lost 2 years	71.4 (n = 26)	53.1 (n = 27)	
BMI 1 year	29.6	31.1	
BMI 2 years	28.5	31.9	

TABLE 22 *Summary of results: gastric bypass versus vertical banded gastroplasty – weight change (continued)*

VanWoert, 1992[106]	*GBP (n = 15)*	*VBG (n = 17)*	
% ideal body weight at 3 years	121%	123%	*p* = ns
MacLean, 1995, 1993[121,122]	*RYGBP (n = 52)*	*VBG (n = 54)*	
Success rate[b] ~ 3 years	30 (58%)	21 (39%)	*p* = 0.08
Success rate up to 6.5 years	16 (34%)	9 (16%)	*p* = 0.112

BMI, body mass index; GBP, gastric bypass; LRYGBP, laparoscopic Roux-en-Y gastric bypass; LVBG, laparoscopic vertical banded gastroplasty; RYGBP, Roux-en-Y gastric bypass; VBG, vertical banded gastroplasty.
All mean (± SD) unless stated.
a Data estimated from figure.
b Success defined as BMI < 35 or < 50% excess weight and no reoperation.

reported no deaths.[106,108,109,120–122,124] Three of these trials were comparisons of open procedures,[106,120–122] the other two were comparisons of laparoscopic procedures.[108,109,124] One trial reported no deaths in the vertical banded gastroplasty group but two deaths (10%) in the gastric bypass group, occurring after three days and 13 months as the result of assumed arrhythmia.[123] Agren and Naslund[73] reported one death, but did not state when this occurred or whether following gastric bypass, vertical banded gastroplasty or gastric banding (unbanded, intervention not included in systematic review) (*Table 24*).

Complications were not reported by all studies, but when they were reported they differed between the various surgical procedures (*Table 24*).

Of the two studies that compared laparoscopic procedures, Olbers and colleagues[108,109] reported no conversions to open surgery, but Lee and

colleagues[124] reported that conversion to open surgery occurred in one (2.5%) patient with laparoscopic gastric bypass and none of the patients with laparoscopic vertical banded gastroplasty (*p* = ns). Operative time was significantly less with laparoscopic vertical banded gastroplasty in both studies [126 minutes (SD 38) versus 209 minutes (SD 50), *p* < 0.001[124], and 105 minutes (SD 35) versus 138 minutes (SD 41), *p* < 0.001[108,109]]. In one study mean postoperative stay was also significantly shorter for the laparoscopic vertical-banded gastroplasty group [3.5 days (0.9) versus 5.7 days (2.2), *p* < 0.001[124]], whereas in the other study there appeared to be little difference in the length of hospital stay (LOS) [median three days (range 1–16 days) versus three days (range 2–15 days)[108,109]].

In one study[124] early postoperative complications were significantly more common following laparoscopic gastric bypass (17.5%, seven patients)

TABLE 23 *Summary of results: gastric bypass versus vertical banded gastroplasty – QoL*

Lee, 2004[124]	**LRYGBP (*n* = 40)**	**LVBG (*n* = 40)**	**_p_-value**
Mean GIQLI domain score at 12 months:			
Symptoms (baseline 63.7)	60.9	54.3	
Physical function (baseline 16.1)	24	20.9	
Emotional function (baseline 12.8)	17.7	14.7	
Social function (baseline 14.3)	18.4	16.5	
Overall score (baseline 106.9)	121	106.4	

GIQLI; gastrointestinal quality of life index; LRYGBP, laparoscopic Roux-en-Y gastric bypass; LVBG, laparoscopic vertical banded gastroplasty.
Baseline data reported for both groups combined only. GIQLI scored 0–4 (worst–best), maximum score 144.

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than laparoscopic vertical banded gastroplasty (2.5%, one patient). Three of the seven early postoperative complications experienced by laparoscopic gastric bypass patients were major complications. These required interventional management and hospitalisation for over 14 days. Two with anastomotic leakage required reoperation, the third had an abdominal abscess. The remaining four early postoperative complications in this group were classed as minor and included upper gastrointestinal bleeding, a sutured nasogastric tube, and minor leakage from a drainage tube. Only one early postoperative complication occurred in the laparoscopic vertical banded gastroplasty group and this was a wound infection that was classed as a minor complication. Analgesic use was also higher [2.4 units (3.0) versus 1.4 units (1.5), respectively ($p < 0.05$)] in this study.[124] The second study that compared laparoscopic procedures[108,109] reported five early reoperations in the gastric bypass group (three for haemorrhage, one for stenosis and one for suspected leak) and one early reoperation in the vertical banded gastroplasty group (for suspected leak), but this difference was not significant ($p = 0.080$). A statistical comparison of the perioperative complications reported by Olbers and colleagues[108,109] (in addition to the reoperations) is not provided, but these appear similar (gastric bypass group: two minor bleeding, one deep infection; vertical banded gastroplasty group: four minor bleeding, one deep infection) (*Table 24*). Neither group experienced a thrombotic complication, and there was no difference in the incidence of pulmonary complications between the groups ($p = 0.888$). One patient in the laparoscopic Roux-en-Y gastric bypass group experienced an intra-abdominal abscess after discharge.

Readmission for late complications reported by Lee and colleagues[124] was similar between the laparoscopic procedures (10% versus 5%, $p = $ ns). Late complications associated with laparoscopic gastric bypass included marginal ulcer requiring blood transfusion (two patients), anastomotic stricture (one patient), and pyothorax (pus in the chest cavity) (one patient). Two patients (5%) with laparoscopic vertical banded gastroplasty experienced the late complication of reflux oesophagitis, one of which required laparoscopic revision surgery. Olbers and colleagues,[108,109] however, reported that remedial surgical intervention was required for eight participants in the vertical banded gastroplasty group (four in the first year and four in the second year, all conversion to Roux-en-Y gastric bypass, due to: one

migration of outlet restricting band, five vomiting and insufficient weight loss, two vomiting and excessive weight loss), but for none in the gastric bypass group.

In the comparisons of open procedures[73,106,120–123] gastric bypass patients suffered from symptomatic ulcer disease (25% of patients),[120] staple-line fistula (23%),[121,122] stomal ulcers (13% of patients),[121,122] intractable vomiting and stomal stenosis (25%),[123] marginal ulcer of jejunal side of gastrojejunostomy (5%),[123] cholelithiasis (gallstone formation) (13%),[106] and peptic gastro-oesophagitis (33%).[106] Vertical banded gastroplasty patients suffered stenosis (20%),[121,122] enlarged orifice (13%),[121,122] staple-line fistula (4%),[121,122] clinical failure (4%),[121,122] abscess (2%),[121,122] superficial stomal erosions (5%),[123] cholelithiasis (24%)[106] and peptic gastro-oesophagitis (18%).[106] Intraoperative cholecystectomy and postoperative cholecystectomy were reported for gastric bypass (20% and 29% respectively) and vertical banded gastroplasty (14% and 29% respectively) (*Table 24*).[120]

In the trial by MacLean and colleagues,[121,122] failures of vertical banded gastroplasty (due to stenosis and enlargement of the gastroplasty orifice), and failures of gastric bypass (due to perforation of the vertical staple line), were converted to normal (9% versus 2%) or isolated gastric bypass (44% versus 37%). In another trial by Sugerman and colleagues,[123] a total of four (20%) vertical banded gastroplasty patients were converted to Roux-en-Y gastric bypass. One patient was converted at one month due to staple-line disruption, and a further three patients were converted due to a failure to lose weight, one at 18 months, and two at 38 months following surgery. After 2 years there were no significant deficiencies in most vitamins, electrolytes, renal or liver function tests. However, vitamin B_{12} levels were lower in patients with Roux-en-Y gastric bypass than those with vertical banded gastroplasty (286 pg/ml versus 461 pg/ml, p<0.05) (Appendix 6). Agren and Naslund[73] found just one patient (4%) with vertical banded gastroplasty required reoperation for staple-line disruption. Agren and Naslund[73] reported that morbidity was low and not significantly different between the groups, but no data were presented.

Summary
Seven RCTs were included. Six trials were of uncertain risk of bias as many factors were not reported. One study by Sugerman and colleagues had a high risk of bias because of an a priori

TABLE 24 *Summary of results: gastric bypass versus vertical banded gastroplasty – complications and additional procedures*

Howard, 1995[120]	*GBP (n = 20)*	*VBG (n = 22)*	*p-value*
Deaths	0	0	
Early complication: wound infection	1 (2%) super-obese patient		
Late complication: symptomatic ulcer disease	25% (half required surgical intervention)	0%	
Intraoperative cholecystectomy[a]	20%	14%	
Late complication: postoperative cholecystectomy	29%	29%	
Sugerman, 1987[123]	*RYGBP (n = 20)*	*VBG (n = 20)*	
Deaths	2/20 (10%)	0	
Conversions VBG to RYGBP		1/20 (5%) at 1 month; 1/20 (5%) at 18 months; 2/20 (10%) at 38 months	
Intractable vomiting and stomal stenosis	5/20 (25%)		
Marginal ulcer of jejunal side of gastrojejunostomy	1/20 (5%)		
Superficial stomal erosion		1/20 (5%)	
Vitamin B_{12} at 24 months, pg/ml [mean (SD)]	286 ($\pm$ 149)	461 ($\pm$ 226)	$p < 0.05$
Olbers, 2005[108,109]	*LRYGBP (n = 37)*	*LVBG (n = 46)*	
Deaths	0	0	
Conversions to open surgery	0	0	
Operating time [mean (SD)]	138 ($\pm$ 41) minutes	105 ($\pm$ 35) minutes	$p < 0.001$
Early reoperation (*n*)	5	1	$p = 0.080$
Haemorrhage	3	0	
Stenosis	1	0	
Suspected leak	1	1	
Perioperative complications (*n*)[b]			
Minor bleeding	2	4	
Deep infection	1	1	
Thrombotic complications	0	0	
Pulmonary complications	States no difference between groups		$p = 0.888$
Median hospital stay, days	3 (range 2–15)	3 (range 1–16)	
Remedial surgical intervention (*n*, conversion to RYGBP)	0	8	
Due to migration of outlet restricting band		1	
Vomiting and insufficient weight loss		5	
Vomiting and excessive weight loss		2	
Intra-abdominal abscess after discharge (*n*)	1	0	

TABLE 24 *Summary of results: gastric bypass versus vertical banded gastroplasty – complications and additional procedures (continued)*

Agren and Naslund, 1989[73]	*Loop GBP (n = 25)*	*VBG (n = 27)*	
Deaths		1 (group not stated[c])	
Reoperation		1/27 (4%)	
Lee, 2004[124]	*LRYGBP (n = 40)*	*LVBG (n = 40)*	
Deaths	0	0	p = ns
Conversions to open surgery	1/40 (2.5%)	0	p = ns
Mean operative time (minutes)	209 ($\pm$ 50)	126 ($\pm$ 38)	$p < 0.001$
Intraoperative blood loss (ml)	35 ($\pm$ 26)	31 ($\pm$ 77)	p = ns
Postoperative flatus passage (days)	2.5 ($\pm$ 1.2)	1.9 ($\pm$ 0.6)	$p < 0.01$
Early postoperative complication	7/40 (17.5%)	1/40 (2.5%)	$p < 0.05$
Major early complication (*n*)[d]	3	0	
Anastomotic leakage	2 (reoperation)		
Abdominal abscess	1		
Minor early complication (*n*)	4	1	
Included upper gastrointestinal bleeding, a sutured nasogastric tube, and minor leakage from a drainage tube	4		
Wound infection		1	
Analgesic use (units)	2.4 ($\pm$ 3.0)	1.4 ($\pm$ 1.5)	$p < 0.05$
Postoperative stay (days)	5.7 ($\pm$ 2.2)	3.5 ($\pm$ 0.9)	$p < 0.001$
Late complications (readmission)	4/40 (10%)	2/40 (5%)	p = ns
Anastomotic stricture	1		
Marginal ulcer	2		
Pyothorax	1		
Reflux oesophagitis		2 (1 laparoscopic revision surgery)	
VanWoert, 1992[106]	*GBP (n = 15)*	*VBG (n = 17)*	
Deaths	0	0	
Major late complication: cholelithiasis	13%	24%	
Major late complication: peptic gastro-oesophagitis	33%	18%	
MacLean, 1995, 1993[121,122]	*RYGBP (n = 52)*	*VBG (n = 54)*	
Deaths	0	0	
Conversions at approx. 3 years	0 to normal; 12/52 (23%) to IGBP	5/54 (9%) to normal; 18/54 (33%) to IGBP	
Conversions up to 6.5 years	1/52 (2%) to normal; 19/52 (37%) to IGBP.	5/54 (9%) to normal; 24/54 (44%) to IGBP	
Reoperations	12/52 (23%)	23/54 (43%)	
Stenosis	0	11 (20%)	
Enlarged orifice	0	7 (13%)	
Staple-line disruption	12 (23%)	2 (4%)	
Clinical failure	0	2 (4%)	
Stomal ulcer[e]	7 (13%)	0	
Abscess	0	1 (2%)	

TABLE 24 *Summary of results: gastric bypass versus vertical banded gastroplasty – complications and additional procedures (continued)*

GBP, gastric bypass; IGBP, isolated gastric bypass; LRYGBP, laparoscopic Roux-en-Y gastric bypass; LVBG, laparoscopic vertical banded gastroplasty; ns, not statistically significant; RYGBP, Roux-en-Y gastric bypass; SD, standard deviation; VBG, vertical banded gastroplasty.
a   For pre-existing gall bladder disease.
b   Perioperative complications in addition to conversions to open surgery and reoperations.
c   Agren and Naslund 1989[73], also included a third trial arm, non-adjustable gastric banding, that was not eligible for inclusion in this systematic review. The death may have occurred in any of the three trial arms.
d   Major complications required interventional management and hospitalisation of over 14 days.
e   RYGBP patients with stomal ulcer were among the 12 patients with staple-line disruption.

stopping rule. On measures of weight, participants who underwent gastric bypass had a better outcome, particularly at later time points, in five of the seven trials than those who underwent vertical banded gastroplasty (although a statistically significant difference was only reported in three of these trials). Only Lee and colleagues reported on QoL, which they found to be better for the gastric bypass group. Data on comorbidities were not assessed. Reporting of complications varied between studies. Evidence from two studies[108,109,124] suggests that the laparoscopic vertical banded gastroplasty surgery is quicker, and is associated with fewer early postoperative complications than laparoscopic gastric bypass surgery. However, two studies of open surgery[121–123] report that after approximately three years, conversions to an alternative bariatric procedure occurred more often in the vertical banded gastroplasty groups, but neither study tested this for statistical significance.

Gastric bypass (non-banded) versus banded gastric bypass

One RCT[118] compared non-banded long limb gastric bypass with banded long limb gastric bypass in participants with BMI greater than 50. Banded gastric bypass (which is not undertaken in the UK) is considered separately in this review, although there is some disagreement among surgeons about whether it constitutes a distinct procedure, or whether it is a variation of the standard gastric bypass procedure.

Weight change

At one and two years follow-up, Bessler and colleagues[118] reported per cent excess weight loss was greater for participants undergoing banded than non-banded long limb gastric bypass, but the differences were not statistically significant (*Table 25*). After three years, the per cent excess weight loss was statistically significantly higher in the banded gastric bypass group compared with the non-banded gastric bypass group (*p* < 0.05).

There is however an uncertain risk of bias for this outcome as the paper reports that this was based on the small number of patients reaching the 36-month follow-up period (numbers not presented). The proportion achieving a BMI of less than 35 was higher in the banded gastric bypass groups than the non-banded gastric bypass groups at one and two years follow-up but the difference was not statistically significant. No rates were reported for the three-year follow-up.

Quality of life and comorbidities

Data on QoL were not assessed. Comorbidities were reported by Bessler and colleagues.[118] The study reported baseline values for stated comorbidities and the proportion with resolution of these comorbidities; however, the study does not state which follow-up period is being reported, or give any numerators and denominators for these calculations.

The proportion of participants with resolution of their respective comorbidities was not shown to be statistically significantly different between the two interventions (*Table 26*).

Complications and additional operative procedures

There were no deaths reported in the study by Bessler and colleagues[118] and no statistically significant differences between banded gastric bypass and non-banded gastric bypass in rates of any postoperative complications. Postoperative gastrointestinal symptoms were scored according to a subjective scale where 0 = none, 1 = mild, 2 = moderate, 3 = severe. In this study only the scores for emesis were statistically significantly better (lower score) in the non-banded gastric bypass group than in the banded gastric bypass participants (0.35 versus 0.13 respectively, *p* = 0.0002) (*Table 27*). No other gastrointestinal symptoms were statistically significantly different between the two interventions. The proportion of

TABLE 25 *Summary of results: gastric bypass (non-banded) versus banded gastric bypass – weight change*

Bessler, 2007[118]	Banded GBP (*n* = 46)	Non-banded GBP (*n* = 44)	*p*-value
% EWL at 12 months	64	57.4	*p* = ns
% EWL at 24 months	64.2	57.2	*p* = ns
% EWL at 36 months	73.4 (small *n*, not reported)	57.7 (small *n*, not reported)	*p* < 0.05
Achieving a BMI of < 35 at 12 months (%):	47.8	41.0	
Achieving a BMI of < 35 at 24 months (%)	52.9	37.5	
BMI, body mass index; EWL, excess weight loss; GBP, gastric bypass; ns, not statistically significant.			

TABLE 26 *Summary of results: gastric bypass (non-banded) versus banded gastric bypass – comorbidities*

Bessler, 2007[118]	Banded GBP (*n* = 46)	Non-banded GBP (*n* = 44)	*p*-value
Resolution of hypertension (%)	79	90	*p* = ns
Resolution of diabetes (%)	92	98	*p* = ns
Resolution of hyperlipidaemia (%)	50	62	*p* = ns
Resolution of arthritis (%)	76	91	*p* = ns
Resolution of gastro-oesophageal reflux disease (%)	94	83	*p* = ns
Resolution of stress urinary incontinence (%)	83	93	*p* = ns
GBP, gastric bypass; ns, not statistically significant.			

TABLE 27 *Summary of results: gastric bypass (non-banded) versus banded gastric bypass – complications and additional procedures*

Bessler, 2007[118]	Banded GBP (*n* = 46)	Non-banded GBP (*n* = 44)	*p*-value
Mortality	0	0	
Total complications	12/46 (26%)	13/44 (29.5%)	*p* = ns
Wound infection	7/46 (15.2%)	5/44 (11%)	*p* = ns
Anastomotic leak	0	2/44 (4.8%)	*p* = ns
Pneumonia	1/46 (2.1%)	1/44 (2.2%)	*p* = ns
Pulmonary embolism	0	0	
Small bowel obstruction	1/46 (2.1%)	1/44 (2.2%)	*p* = ns
Band erosion/slippage/removal	0	n/a	
Other	3/46 (6.5%)	4/44 (9.0%)	*p* = ns
Gastrointestinal symptoms (average scores)			
Dumping	0.12	0.05	*p* = ns
Emesis	0.35	0.13	*p* = 0.0002
Diarrhoea	0.11	0.13	*p* = ns
Constipation	0.07	0.08	*p* = ns
Flatulence	0.22	0.13	*p* = ns
Abdominal pain	0.04	0.06	*p* = ns
Food intolerance (%)	79	33	*p* < 0.05
GBP, gastric bypass; ns, not statistically significant.			

participants with food intolerance was higher in the banded gastric bypass group (79% versus 33%, $p < 0.05$). Care is required in the interpretation of these results, not only because of the subjective nature of these outcomes, but also because the study does not state which follow-up period is being reported or what the participant numbers were for these outcomes.

Summary
One study (with a low risk of selection bias but at high risk of bias through selective reporting) found similar weight loss after banded and non-banded gastric bypass in people with BMI greater than 50. Although a statistically significant difference in BMI was found at 36 months follow-up, this was based on a small number of participants. Rates of improvement of existing comorbidities were not different between the two groups and complications were also generally similar. The evidence suggests that in these high BMI participants there is little added benefit from the addition of banding to the intervention.

Laparoscopic gastric bypass versus laparoscopic adjustable gastric banding
One RCT[119] compared laparoscopic Roux-en-Y gastric bypass with laparoscopic adjustable gastric banding.

Weight change
At one and three years of follow-up Angrisani and colleagues[107] found that the per cent excess weight loss was greater for those undergoing laparoscopic Roux-en-Y gastric bypass than laparoscopic adjustable gastric banding, but no statistical significance was reported (*Table 28*). After 5 years of follow-up the per cent excess weight loss and mean weight were statistically significantly better for participants in the laparoscopic Roux-en-Y gastric bypass group compared with those in the laparoscopic adjustable gastric banding group ($p < 0.001$ for both outcomes). At one and three years follow-up the mean BMI was also lower in the laparoscopic Roux-en-Y gastric bypass group (but no p-values were reported) than the laparoscopic adjustable gastric banding group. After five years the mean BMI was statistically significantly better in the laparoscopic Roux-en-Y gastric bypass group than the laparoscopic adjustable gastric banding group ($p < 0.001$). The proportion classed as weight loss failures, defined as those with a BMI > 35 at 5 years, were statistically significantly lower in the laparoscopic Roux-en-Y gastric bypass than the laparoscopic adjustable gastric banding group ($p < 0.001$) and the proportion with a BMI of less than 30 at 5 years were statistically significantly

higher in the laparoscopic Roux-en-Y gastric bypass group ($p < 0.001$) than in the laparoscopic adjustable gastric banding group.

Quality of life and comorbidities
QoL was not assessed by Angrisani and colleagues.[107] Baseline rates of comorbidities were low in this study, with two participants in the laparoscopic Roux-en-Y gastric bypass group having hyperlipaemia, one hypertension and one Type 2 diabetes. In the laparoscopic adjustable gastric banding group three participants had hypertension and one sleep apnoea. The study reports that at five years there was resolution of the diabetes and hyperlipaemia (in the laparoscopic Roux-en-Y gastric bypass group) and the sleep apnoea (in the laparoscopic adjustable gastric banding group) (Appendix 8).

Complications and additional operative procedures
No deaths were noted in either group of the Angrisani and colleagues study[119] (*Table 29*). Operative time for laparoscopic adjustable gastric banding was significantly shorter than for laparoscopic Roux-en-Y gastric bypass [mean 60 (SD 20) minutes versus mean 220 (SD 100) minutes, $p < 0.001$]. Four (15.2%) participants in the laparoscopic adjustable gastric banding group underwent a reoperation (two pouch dilatation, two band removal because of inadequate weight loss: one of these was converted to biliopancreatic diversion, three waiting list for laparoscopic Roux-en-Y gastric bypass) and three (12.5%) from the laparoscopic Roux-en-Y gastric bypass group underwent a reoperation (for potentially lethal complications not further specified). Early complications requiring surgery in the laparoscopic Roux-en-Y gastric bypass group occurred in two (8.4%) [one posterior pouch leak intraoperatively causing conversion to open surgery, one (4.2%) sepsis caused by jejunal perforation (sutured and intestine resected)]. No early complications requiring surgery were noted in the laparoscopic adjustable gastric banding group. One participant undergoing laparoscopic Roux-en-Y gastric bypass had a late complication (small bowel obstruction as the result of internal hernia) and two participants undergoing laparoscopic adjustable gastric banding had gastric pouch dilatation (which was treated by band removal). No significance testing was undertaken for reoperation rates, or early or late complication rates between groups. Mean hospital stay was statistically significantly longer in the laparoscopic Roux-en-Y gastric bypass group than the laparoscopic adjustable gastric banding group [4 days (SD 2) versus 2 days (SD 1) for the

TABLE 28 *Summary of results: laparoscopic gastric bypass versus laparoscopic adjustable gastric banding – weight change*

Angrisani, 2007[107]	LAGB (*n* = 27)	LRYGBP (*n* = 24)	*p*-value
% excess weight loss at 12 months	34.7	51.3	
% excess weight loss at 36 months	47.3	67.3	
% excess weight loss at 5 years (range 60–66 months)	47.5	66.6	$p < 0.001$
Mean weight (kg) at 12 months	102.4	92.8	
Mean weight (kg) at 36 months	98.7	83.5	
Mean weight (kg) at 5 years (range 60–66 months)	97.9	84	$p < 0.001$
Mean BMI at 12 months	38.7	35.4	
Mean BMI at 36 months	35.6	29.1	
Mean BMI at 5 years (range 60–66 months)	34.9	29.8	$p < 0.001$
Weight loss failure (BMI > 35 at 5 years)	9/26 (34.6%)	1/24 (4.2%)	$p < 0.001$
BMI < 30 at 5 years	3/26 (11.5%)	15/24 (62.5%)	$p < 0.001$

BMI, body mass index; LAGB, laparoscopic adjustable gastric banding; LRYGBP, laparoscopic Roux-en-Y gastric bypass.

two groups respectively, $p < 0.05$], although one participant in the laparoscopic Roux-en-Y gastric bypass group required an intensive care stay of 40 days (Appendix 8).

Summary
On a variety of measures of weight this small study showed that laparoscopic Roux-en-Y gastric bypass was superior to laparoscopic adjustable gastric banding. Reoperation rates were similar between the two interventions, and comorbidities were similar and few. Early complications requiring reoperation were seen in more participants undergoing laparoscopic Roux-en-Y than laparoscopic adjustable gastric banding, but the numbers were small and not tested for statistical significance. The risk of bias for this study is uncertain, although the risk of bias

TABLE 29 *Summary of results: laparoscopic gastric bypass versus laparoscopic adjustable gastric banding – complications and additional procedures*

Angrisani, 2007[107]	LAGB (*n* = 27)	LRYGBP (*n* = 24)	*p*-value
Mortality	0	0	
Reoperation[a]	4/26 (15.2%)	3/24 (12.5%)	
Gastric pouch dilatation	2		
Unsatisfactory weight loss (band removal)	2		
Early complications (with reoperation)	0	2 (8.4%)	
Posterior pouch leak		1 (conversion to open)	
Sepsis (jejunal perforation)	0	1	
Late complication	2/26 (7.6%)	1/24 (4.2%)	
Small bowel obstruction due to internal hernia		1	
Pouch dilatation (band removal)	2		
Hospital stay, days [mean (SD)]	2 (± 1)	4 (± 2)	$p < 0.05$
Operative time, mins [mean (SD)]	60 (± 20)	220 (± 100)	$p < 0.001$

LAGB, laparoscopic adjustable gastric banding; LRYGBP, laparoscopic Roux-en-Y gastric bypass; SD, standard deviation.
a   LAGB group: one conversion to biliopancreatic diversion, other three went on to waiting list for LRYGBP. LRYGBP reoperations were each for a potentially lethal complication (unspecified).

from incomplete outcome data for weight loss and comorbidities is likely to be low.

Laparoscopic gastric bypass versus laparoscopic sleeve gastrectomy

One RCT compared laparoscopic Roux-en-Y gastric bypass with laparoscopic sleeve gastrectomy.[125]

Weight loss

There were no statistically significant differences in BMI or weight loss between the two procedures at 12 months follow-up. However, laparoscopic sleeve gastrectomy led to a greater per cent excess weight loss at 12 months [69.7% (SD 14.6) versus 60.5% (SD 10.7), $p = 0.05$] in this small RCT (*Table 30*).

Quality of life and comorbidities

QoL was not assessed by this study. Two patients had diabetes at baseline (both in the laparoscopic Roux-en-Y gastric bypass group); this was resolved at 12 months in both patients. The outcome of other comorbidities noted at baseline (see Appendix 9) was not reported.

Complications and additional operative procedures

Karamanakos and colleagues reported that there were no conversions to open surgery and no intraoperative and postoperative complications. No further details were reported.

Summary

In this small RCT with uncertain risk of bias, BMI and weight loss at 12 months follow-up were similar between laparoscopic Roux-en-Y gastric bypass and sleeve gastrectomy. Per cent excess weight loss was greater with sleeve gastrectomy at 12 months ($p = 0.05$).

Vertical banded gastroplasty versus adjustable gastric banding

One study[126] compared open vertical banded gastroplasty with open adjustable gastric banding, one study[110] compared laparoscopic vertical banded gastroplasty with laparoscopic adjustable silicone gastric banding, and one study[127,128] compared open vertical banded gastroplasty with laparoscopic adjustable banding.

Weight change

At one year follow-up, Nilsell and colleagues[126] found that weight loss was greater for the vertical banded gastroplasty group, but these patients then began to regain weight. The patients with adjustable gastric banding experienced lower initial weight loss, but this continued over five years resulting in a weight reduction of 43 kg at five years compared with 35 kg for vertical banded gastroplasty (statistical significance not given) (*Table 31*).

When comparing laparoscopic procedures, Morino and colleagues[110] also found significantly lower BMI with vertical banded gastroplasty at one year follow-up (30.1 versus 35.5, $p < 0.05$), but at two and three years follow-up the difference was not statistically significant (two years: 29.7 versus 34.8; three years: 30.7 versus 35.7). A similar result was seen in terms of percentage excess weight loss which was significantly greater with vertical banded gastroplasty at one year follow-up (62.3% versus 39.2%, $p < 0.05$), but was not statistically significantly different at later follow-up (two years: 63.5% versus 41.4%, three years: 58.9% versus 39.0%, p-values not reported). At three years follow-up, 25% of patients with laparoscopic adjustable silicone gastric banding and 63% of patients with laparoscopic vertical banded gastroplasty had an excellent or good result (residual excess weight < 50%, $p = 0.056$).

Van Dielen and colleagues[127,128] reported a comparison of open vertical banded gastroplasty and laparoscopic adjustable gastric banding at one and two years follow-up, with data at a mean of 84 months follow-up reported in a recent abstract[128] (*Table 31*). At one year, mean BMI was lower in the open vertical banded gastroplasty group than in the laparoscopic adjustable gastric banding group [31.1 (SD 6.2) versus 35.0 (SD 6.3), no p-value reported] and statistically significantly lower at the two-year follow-up [31.0 (SD 6.0) versus 34.6 (SD 6.5), $p \leq 0.002$]. Percentage excess weight loss was statistically significantly greater in the open vertical banded gastroplasty group in comparison to the laparoscopic adjustable gastric banding group at both one and two years [one year: 71.1% (SD 24.0) versus 53.3% (SD 21.2), $p \leq 0.001$; two years: 70.1% (SD 25.5) versus 54.9% (SD 23.3), $p \leq 0.001$]. The difference was maintained at a mean of 84 months follow-up (per cent excess BMI loss 68.8% versus 56.9%, respectively).[128] However, it should be noted that at this time point 59% of vertical banded gastroplasty participants had been converted to gastric bypass, and 11% of laparoscopic adjustable gastric banding participants had been converted to another procedure. From the limited information presented in the abstract reporting these results[128] it is not clear whether this has been taken into consideration.

TABLE 30 *Summary of results: laparoscopic Roux-en-Y gastric bypass versus laparoscopic sleeve gastrectomy – weight change*

Karamanakos, 2008[125]	LRYGBP (*n* = 16)	LSG (*n* = 16)	*p*-value
BMI at 12 months	31.5 (± 3.4)	28.9 (± 3.6)	*p* = 0.41
% EWL at 12 months	60.5 (± 10.7)	69.7 (± 14.6)	*p* = 0.05
Weight loss at 12 months (kg)	40.0 (± 8.3)	43.6 (± 11.7)	*p* = 0.322

BMI, body mass index; EWL, excess weight loss; LRYGBP, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy.
All mean (± SD).

Quality of life and comorbidities

One study assessed patient satisfaction[126] and one study reported on comorbidities,[127] whereas one study did not report QoL or comorbidity outcomes.[110] At five years follow-up, patients were asked if they were satisfied with, or regretted having undergone, the operation.[126] Only 56% of vertical banded gastroplasty patients were satisfied with the result of the operation, while 81% of the patients with adjustable gastric banding were satisfied (statistical significance not given). The comparison of open vertical banded gastroplasty and laparoscopic adjustable gastric banding[127] revealed that although the overall number of patients with comorbidity in both groups significantly decreased following surgery at one and two years follow-up, no differences in comorbidities were observed between groups (open vertical banded gastroplasty: 82% at baseline, 30.4% at one year, 47.9%, at two years, *p* ≤ 0.001 versus baseline; laparoscopic adjustable gastric banding 78% at baseline, one year 37.5% at one year, 40% at two years, *p* ≤ 0.001 versus baseline) (*Table 32*). Significant improvements in both groups were seen in joint problems (*p* ≤ 0.001 compared with preoperative), pulmonary problems (*p* ≤ 0.05 compared to preoperative) and diabetes mellitus (*p* ≤ 0.05 compared with preoperative). No improvement in either group was observed between the percentage of patients with preoperative and postoperative hypertension, cardiovascular problems, hypercholesterolaemia, reflux disease, sleep apnoea or neurological problems (Appendix 10). After a mean of 84 months follow-up comorbidities had all significantly decreased except for gastro-oesophageal reflux disease (GERD), which increased in both groups, although no numerical data are provided in the abstract reporting these results.[128]

Complications and additional operative procedures

Van Dielen and colleagues[127] report that two deaths (4%) occurred, both in the open vertical banded gastroplasty group, one from sepsis in the first postoperative week, and one as the result of a pre-existing pneumonia that had not been reported to the surgeon preoperatively. No postoperative deaths occurred in the other two studies,[110,126] and although one patient from each group died during follow-up in the study by Nilsell and colleagues,[126] these deaths are reported to be unrelated to the surgery (*Table 33*).

Operative time was shorter with laparoscopic adjustable silicone gastric banding than laparoscopic vertical banded gastroplasty [65.4 minutes (35–120) versus 94.2 minutes (40–270), *p* < 0.05], as was hospital stay [3.7 days (2 to 6), versus 6.6 days (3 to 58), *p* < 0.05] in the Morino and colleagues study.[110] Hospital stay was also shorter for laparoscopic adjustable gastric banding than open vertical banded gastroplasty [mean 3.5 days (SD 1.5), range 2–9 days, versus mean 6.8 days (SD 10.4) days, range 2–56 days; *p* < 0.001] in the study by van Dielen and colleagues.[127]

One reoperation on the third postoperative day because of an anastomotic leak in the vertical banded gastroplasty group is reported by Nilsell and colleagues.[126] Morino and colleagues[110] found that early morbidity was similar between the two laparoscopic procedures (laparoscopic adjustable gastric banding 6.1% versus laparoscopic vertical gastric banding 9.8%, *p* = 0.754) and there were no conversions to open surgery. One patient experienced early postoperative band slippage (laparoscopically repositioned). There was also one port infection and one haematoma at the port site in the laparoscopic adjustable gastric banding group. In the vertical banded gastroplasty group there was one fistula at the staple line (treated with open gastric bypass), two instances of prolonged postoperative pyrexia, and two respiratory failures without evidence of pulmonary embolism. Van Dielen and colleagues[127] reported that two conversions to open surgery were necessary in the laparoscopic adjustable banding group, and

TABLE 31 *Summary of results: vertical banded gastroplasty versus adjustable gastric banding – weight change*

Nilsell, 2001[126]	VBG (n = 30)	AGB (n = 29)	p-value
Mean weight (kg) baseline (SEM)	123 (30)	124 (29)	
Mean weight (kg) 1 year (SEM)[a]	82 (25)	98 (28)	
Mean weight (kg) 2 year (SEM)[a]	85 (29)	88 (23)	
Mean weight (kg) 3 year (SEM)[a]	90 (15)	85 (13)	
Mean weight (kg) 4 year (SEM)[a]	95 (15)	86 (17)	
Mean weight (kg) 5 years (SEM)	88 (16)	81 (16)	
Morino, 2003[110]	**LVBG (n = 51)**	**LAGB (n = 49)**	
BMI 1 year	30.1	35.5	$p < 0.05$
BMI 2 years	29.7	34.8	$p = ns$
BMI 3 years	30.7	35.7	$p = ns$
% excess weight loss 1 year	62.3	39.2	$p < 0.05$
% excess weight loss 2 years	63.5	41.4	$p = ns$
% excess weight loss 3 years	58.9	39.0	$p = ns$
Patients with an excellent or good result[b] 2 years	74%	35%	$p < 0.001$
Patients with an excellent or good result 3 years	63%	25%	$p = 0.056$
van Dielen, 2005[127,128]	**Open VBG (n = 50)**	**LAGB (n = 50)**	**p-value**
Mean BMI at 1 year (± SD)	31.1 (± 6.2)	35.0 (± 6.3)	
Mean BMI at 2 years (± SD)	31.0 (± 6.0)	34.6 (± 6.5)	$p \leq 0.002$
% excess weight loss at 1 year (± SD)	71.1 (± 24.0)	53.3 (± 21.2)	$p \leq 0.001$
% excess weight loss at 2 years (± SD)	70.1 (± 25.5)	54.9 (± 23.3)	$p \leq 0.001$
% excess BMI loss at mean 84 months	68.8%	56.9%	

BMI, body mass index; AGB, adjustable gastric banding; LAGB, laparoscopic adjustable gastric banding; LVBG, laparoscopic vertical banded gastroplasty; ns, not statistically significant; open, open surgery; SD, standard deviation; VBG, vertical banded gastroplasty.
a Data from figure 2 within Nilsell, 2001.[126]
b Patients with an excellent or good result defined as residual excess weight < 50%.

in an additional patient a conversion to gastric bypass was necessary. In the open vertical banded gastroplasty group nine patients experienced immediate postoperative complications: leakage in three patients required reoperation, two splenectomies were performed, and in two patients an obstruction that necessitated gastroscopy occurred. There were no infections in the laparoscopic adjustable banding group, but there were seven infections in five patients (including the two patients who died) in the open vertical banded gastroplasty group.

Nilsell and colleagues[126] reported that late reoperations were necessary in a third of vertical banded gastroplasty patients because of staple-line disruption with rapid weight regain or strictures of the stoma with vomiting or intolerance of solid

food. The total incidence of staple-line disruption was 18.5% (five patients), but three patients were not reoperated on for various reasons.[126] Three (11.5%) adjustable gastric banding patients were reoperated; two as the result of dilatation of the gastric pouch, and one patient requested that their band be removed for reasons that were unclear. Morino and colleagues,[110] found that late complications were more common following laparoscopic adjustable silicone gastric banding (32.7% versus 14%, $p < 0.05$). However, no patients with laparoscopic vertical banded gastroplasty required late reoperation, whereas 24.5% of patients required late reoperation following laparoscopic adjustable silicone gastric banding ($p < 0.001$), most commonly because of bands slipping. The percentage of late complications occurring in the open vertical banded gastroplasty

TABLE 32 *Summary of results: vertical banded gastroplasty versus adjustable gastric banding – comorbidities*

van Dielen, 2005[127]	Open VBG (n = 50)	LAGB (n = 50)	p-value
Preoperative patients with comorbidity	41 (82%)	39 (78%)	
Joint problems	29 (58%)	28 (56%)	
Pulmonary problems	8 (16%)	9 (18%)	
Hypertension	10 (20%)	7 (14%)	
Diabetes mellitus	7 (14%)	5 (10%)	
Cardiovascular problems	3 (6%)	2 (4%)	
Hypercholesterolaemia	2 (4%)	2 (4%)	
Reflux disease	2 (4%)	3 (6%)	
Sleep apnoea	1 (2%)	1 (2%)	
Neurological problems	0 (0%)	1 (2%)	
At 1 year patients with comorbidity	14 (30.4%)[a]	18 (37.5%)[a]	
Joint problems	7 (15.2%)[a]	10 (20.8%)[a]	
Pulmonary problems	3 (6.5%)[b]	3 (6.3%)[b]	
Hypertension	8 (17.4%)	5 (10.4%)	
Diabetes mellitus	1 (2.2%)[b]	1 (2.1%)[b]	
Cardiovascular problems	2 (4.3%)	2 (4.2%)	
Hypercholesterolaemia	1 (2.2%)	2 (4.2%)	
Reflux disease	0 (0%)	0 (0%)	
Sleep apnoea	0 (0%)	0 (0%)	
Neurological problems	0 (0%)	1 (2.1%)	
At 2 years patients with comorbidity	23 (47.9%)[a]	20 (40%)[a]	
Joint problems	13 (27.1%)[a]	12 (24%)[a]	
Pulmonary problems	3 (6.3%)[b]	1 (2%)[b]	
Hypertension	7 (14.6%)	5 (10%)	
Diabetes mellitus	1 (2.1%)[b]	1 (2%)[b]	
Cardiovascular problems	1 (2.1%)	3 (6%)	
Hypercholesterolaemia	1 (2.1%)	1 (2%)	
Reflux disease	0 (0%)	0 (0%)	
Sleep apnoea	0 (0%)	0 (0%)	
Neurological problems	1 (2.1%)	1 (2%)	

LAGB, laparoscopic adjustable gastric banding; open, open surgery; VBG, vertical banded gastroplasty.
a $p \leq 0.001$ compared to preoperative.
b $p \leq 0.05$ compared to preoperative.

group and the laparoscopic gastric bypass group appear similar in van Dielen and colleagues[127] (no statistical comparison reported). Revisional surgery (conversion to gastric bypass) was necessary in 36% of those who had undergone open vertical banded gastroplasty, in most cases (15/18) this was the result of vertical staple-line disruption. A further eight (16%) patients required a surgical repair of an incisional hernia. Six patients (12%) required gastroscopy at least once for outlet stenosis or

obstruction. In the laparoscopic adjustable gastric banding group, 40% of participants required reoperation. The majority of reoperations (16/20) were major reoperations for pouch dilatation or slippage, band leakage, or band erosion. At a mean of 84 months follow-up, the authors reported that long-term complications 'were mainly' staple-line disruption (51%) and incisional hernia (27%) for patients with open vertical banded gastroplasty, and pouch dilatation (24%) and anterior slippage

(15%) for patients with laparoscopic adjustable gastric banding.[128] Major reoperation was required in 59% of vertical banded gastroplasty patients, who required conversions to gastric bypass, and in 46% of laparoscopic adjustable gastric banding patients, who required refixation or band replacements (35%) or conversion to another procedure (11%).[128]

GERD was slightly more common in patients with vertical banded gastroplasty (14.8%) than adjustable gastric banding (11.5%) in the study by Nilsell and colleagues.[126]

Summary
Three studies were included: one had a low risk of selection bias and two were of uncertain risk of bias for several items, although missing outcome data for weight loss were adequately addressed. Weight loss results were inconclusive. One study found that weight loss was initially greater with vertical banded gastroplasty, but weight regain meant that by three years patients with adjustable gastric banding had a lower mean weight, and this was still the case at five years (statistical significance not reported). The second study found lower BMI and greater per cent excess weight loss following laparoscopic vertical banded gastroplasty, but this was statistically significant only at year one and not at years two or three. The third study found statistically significant lower BMI and greater per cent excess weight loss at one and two years following open vertical banded gastroplasty, and greater per cent excess BMI loss seven years after open vertical banded gastroplasty (statistical significance not reported). However, the impact of participants being converted to another procedure in this study is unclear. More patients who had undergone adjustable gastric banding reported being satisfied with the results at five years, but this apparent superiority was not tested statistically. Resolution of comorbidities was similar in the two groups in the only study that reported on this outcome.[127] It is difficult to draw conclusions regarding complications and additional operative procedures because one study compared two open procedures, one two laparoscopic procedures, and one compared an open procedure with a laparoscopic procedure. In the comparison of open procedures more reoperations were necessary following open vertical banded gastroplasty than open adjustable gastric banding, but a statistical comparison was not reported. Laparoscopic adjustable gastric banding was associated with a statistically shorter operative time and hospital stay than laparoscopic vertical banded gastroplasty, but there were statistically more late complications and reoperations. The third comparison found laparoscopic adjustable gastric banding was associated with a statistically significant shorter hospital stay while open vertical banded gastroplasty led to more infections. Late complications requiring further surgery were similar but a statistical comparison was not reported.

Laparoscopic adjustable gastric banding versus laparoscopic isolated sleeve gastrectomy
One RCT[129] compared laparoscopic adjustable gastric banding with laparoscopic isolated sleeve gastrectomy.

Weight loss
In this study Himpens and colleagues[129] report that the proportion of excess weight loss was statistically significantly greater in participants in the laparoscopic isolated sleeve gastrectomy group than the laparoscopic adjustable gastric banding group at one year (57.7% versus 41.4%, $p = 0.0004$) and three years (66% versus 48% $p = 0.0025$) (*Table 34*). Weight loss (three years: 29.5 kg versus 17 kg, $p < 0.0001$) and reduction in BMI (three years: 27.5 versus 18, $p < 0.0001$) were statistically significantly improved in laparoscopic isolated sleeve gastrectomy participants in comparison with the laparoscopic adjustable gastric banding participants. All of these data were presented by the trial authors as median and range so care should be taken when interpreting the results.

Quality of life and comorbidities
QoL was not assessed in this study. At baseline in the Himpens and colleagues[129] study GERD requiring drug therapy with proton pump inhibitors was a problem for 15% (6/40) of the laparoscopic adjustable gastric banding participants and 20% (8/40) of the participants in the laparoscopic isolated sleeve gastrectomy group. After one year GERD had disappeared in 83% and 75% of these participants in the two groups respectively, and this remained the same at three years. Statistical significance was not reported. In those without GERD at baseline, no statistically significant differences in rates of appearance of GERD between the intervention groups were observed at one year [laparoscopic adjustable gastric banding 3/34 (8.8%), versus laparoscopic isolated sleeve gastrectomy 7/32 (21.8%), $p = $ ns] or three years [laparoscopic adjustable gastric banding 7/34 (20.5%) versus laparoscopic isolated sleeve gastrectomy 1/32 (3.1%), $p = $ ns] (Appendix 11).

TABLE 33 *Summary of results: vertical banded gastroplasty versus adjustable gastric banding – complications and additional procedures*

Nilsell, 2001[126]	*VBG (n = 30)*	*AGB (n = 29)*	*p-value*
Postoperative deaths	0	0	
Deaths	1	1	
Reoperation: anastomotic leak (n)	1	0	
Late reoperations	10/27 (37%)	3/26 (11.5%)	
Removal of band	4	1	
Gastrogastrostomy	3	0	
Longer band	1	0	
Gastric banding	2	0	
Replacement of band	0	2	
Gastro-oesophageal reflux disease	4/27 (14.8%)	3/26 (11.5%)	
Staple-line disruption	5/27 (18.5%)		
Morino, 2003[110]	*LVBG (n = 51)*	*LAGB (n = 49)*	
Mortality	0	0	
Operative time, minutes [mean (range)]	94.2 (40–270)	65.4 (35–120)	$p < 0.05$
Hospital stay, days [mean (range)]	6.6 (3–58)	3.7 (2–6)	$p < 0.05$
Conversion to open surgery	0	0	
Associated procedures	5 (10%)	5 (10%)	
Cholecystectomies	4	5	
Lymph node biopsy	1	0	
Early morbidity	5/51 (9.8%)	3/49 (6.1%)	$p < 0.754$
Band slippage		1	
Port infection		1	
Haematoma at port site		1	
Fistula at staple line	1		
Prolonged postoperative pyrexia	2		
Respiratory failures	2		
Late complications	7/50 (14%)	16/49 (32.7%)	$p < 0.05$
Band slippage		9	
Symptomatic reflux disease	4	3	
Complete food intolerance		1	
Poor compliance		1	
Port infection		1	
Port twisted		1	
Pouch dilatation	1		
Asymptomatic pouch to fundus fistula	1		
Gastric bezoar	1		

TABLE 33 *Summary of results: vertical banded gastroplasty versus adjustable gastric banding – complications and additional procedures (continued)*

Morino, 2003[110]	*LVBG (n = 51)*	*LAGB (n = 49)*	
Late reoperations	0/50	12/49 (24.5%)	*p* < 0.001
Band removed		8	
For slipping		6	
For severe reflux oesophagitis		1	
For poor compliance		1	
Slipped band replaced laparoscopically		1	
Gastric bypass (due to food intolerance)		1	
Port repositioned		1	
Port removed		1	
van Dielen, 2005[127]	*Open VBG (n = 50)*	*LAGB (n = 50)*	
Mortality	2/50 (4%)	0	
Mean length of hospital stay, days (± SD; range)	6.8 (± 10.4; 2–56)	3.5 (± 1.5; 2–9)	*p* < 0.001
Conversion to open surgery	n/a	2 (4%) to open procedure; 1 (2%) to gastric bypass	
Immediate postoperative complications	9/50 (18%)	3 conversions as noted above	
Leakage (reoperation required)	3		
Splenectomy	2		
Obstruction (gastroscopy required)	2		
Infections	7 in 5 (10%) patients	0	
Sepsis[a]	3		
Urinary tract infection	1		
Pneumonia[a]	3		
Wound infection	1		
Late complications requiring further surgery (detailed below)	26/50 (52%)[b]	20/50 (40%)[c]	
Revisional surgery (conversion to gastric bypass)	18/50 (36%)		
Due to vertical staple-line disruption	15		
Due to narrow outlet	2		
Due to insufficient weight loss	1		
Surgical repair of incisional hernia	8/50 (16%)		
Major reoperations		16 (32%)	
Pouch dilatation/pouch slippage		12	
Band leakage		2	
Band erosion		2	
Minor reoperations		4/50 (8%)	
Outlet stenosis or obstruction requiring gastroscopy	6/50 (12%)		

AGB, adjustable gastric banding; LAGB, laparoscopic adjustable gastric banding; LVBG, laparoscopic vertical banded gastroplasty; open, open surgery; VBG, vertical banded gastroplasty.
a A patient with sepsis and a patient with pneumonia account for the two VBG patients who died.
b Proportion who had undergone a major reoperation after a mean follow-up of 84 months had increased to 59%
c Proportion who had undergone a major reoperation after a mean follow-up of 84 months had increased to 46%

TABLE 34 *Summary of results: laparoscopic adjustable gastric banding versus laparoscopic isolated sleeve gastrectomy – weight change*

Himpens, 2006[129]	LAGB (*n* = 40)	LISG (*n* = 40)	*p*-value
% EWL at 1 year (median, range)	41.4 (−11.8 to 130.5)	57.7 (0 to 125.5)	$p = 0.0004$
% EWL at 3 years (median, range)	48 (0 to 124.8)	66 (−3.1 to 152.4)	$p = 0.0025$
Weight loss at 1 year (kg, median, range)	14 (−5 to 38)	26 (0 to 46)	$p < 0.0001$
Weight loss at 3 years (kg, median, range)	17 (0 to 40)	29.5 (1 to 48)	$p < 0.0001$
BMI decrease at 1 year (median, range)	15.5 (5 to 39)	25 (0 to 45)	$p < 0.0001$
BMI decrease at 3 years (median, range)	18 (0 to 39)	27.5 (0 to 48)	$p = 0.0004$

BMI, body mass index; EWL, excess weight loss; LAGB, laparoscopic adjustable gastric banding; LISG, laparoscopic isolated sleeve gastrectomy.

Complications and additional operative procedures

No early postoperative complications were seen in the laparoscopic adjustable gastric banding group of the Himpens and colleagues[129] study, two participants in the laparoscopic isolated sleeve gastrectomy group had an early postoperative complication, both required revisional surgery, in one this was a total gastrectomy for gastric ischaemia (*Table 35*). Late complications requiring surgery were observed in the laparoscopic adjustable gastric banding participants, with three

TABLE 35 *Summary of results: laparoscopic adjustable gastric banding versus laparoscopic isolated sleeve gastrectomy – complications*

Himpens, 2006[129]	LAGB (n = 40)	LISG (n = 40)
Early postoperative complications (requiring surgery)	0	2/40 (5%)
Intraperitoneal bleed requiring laparoscopy		1
Gastric ischaemia requiring total gastrectomy		1
Late complications requiring surgery	7/40 (17.5%)	0
Pouch dilatation leading to band removal	2	
Pouch dilatation leading to conversion to RYGBP	1	
Gastric erosion leading to conversion to RYGBP	1	
Port disconnections, reconnected	3	
Conversion due to insufficient weight loss	2/40 (5%) to RYGBP	2/40 (5%) to laparoscopic duodenal switch
Complications at 1 year (not requiring surgery)		
Shoulder pain	3/40 (7.5%)	
Frequent vomiting	6/40 (15%)	1/40 (2.5%)
Poor choice of alimentation	2/40 (5%)	
Gastric pain		2/40 (5%)
Mineral deficiency		2/40 (5%)
Complications at 3 years (not requiring surgery)[a]		
Shoulder pain	3 (8.5%)	
Frequent vomiting	10 (28.5%)	5 (16.6%)
Poor choice of alimentation	17 (48.5%)	8 (26.6%)
Gastric ulcer	1 (2.8%)	
Mineral deficiency		3 (10%)

LAGB, laparoscopic adjustable gastric banding; LISG, laparoscopic isolated sleeve gastrectomy; RYGBP, Roux-en-Y gastric bypass.
a   To achieve these percentage values the number of participants (denominator) contributing data to the 3-year follow-up for LAGB would have been 35, and for LISG 30.

pouch dilatations (treated with band removal in two and conversion to Roux-en-Y gastric bypass in one); one gastric erosion (treated with Roux-en-Y gastric bypass) and three disconnections of the port (treated with reconnection). There were no late complications requiring surgery in the laparoscopic isolated sleeve gastrectomy group. Complications not requiring surgery that were observed at one and three years can be seen in *Table 35*. There appeared to be higher frequencies of complications in the laparoscopic adjustable gastric banding group than in the laparoscopic isolated sleeve gastrectomy group but this is based on observation of the data only, no statistical analysis was undertaken.

In addition, two participants in each group had 'insufficient weight loss' noted as a complication in the Himpens and colleagues[129] study. The two participants in the laparoscopic adjustable gastric banding group were converted to Roux-en-Y gastric bypass and the two participants in the laparoscopic isolated sleeve gastrectomy group were converted to laparoscopic duodenal switch.

Summary
On measures of weight, participants undergoing laparoscopic isolated sleeve gastrectomy showed more improvement than participants undergoing laparoscopic adjustable gastric banding in one study with an uncertain risk of bias. Rates of complications were observed to be lower in the laparoscopic isolated sleeve gastrectomy group, apart from rates of early postoperative complications.

Open versus laparoscopic gastric bypass
Three RCTs compared open gastric bypass with laparoscopic gastric bypass[113,114,130,131] and another RCT compared open gastric bypass with hand-assisted laparoscopic gastric bypass.[112]

Weight change
Puzziferri and colleagues[113,114] demonstrated a slightly higher percentage of excess body weight loss following laparoscopic gastric bypass (one year: 68%, SD 15) compared with open gastric bypass (one year: 62%, SD 14), but the difference was not statistically significant at one year ($p = 0.07$) or at the three-year or four-year follow-ups[114] (*Table 36*). Similarly, a non-significant difference in reduction of BMI was found at one year by Westling and Gustavsson[131] [laparoscopic 14 (SD 3), open 13 (SD 3)], Sundbom and Gustavsson[112] (BMI reduction of 15 in both groups, BMI: laparoscopic 29, open 30) and at three years

follow-up by Lujan and colleagues[130] (laparoscopic 31, open 35.5). Incomplete weight loss outcome data were adequately addressed by Westling and Gustavsson[131] and by Sundbom and Gustavsson.[112] However, the risk of bias from incomplete weight loss data was uncertain in the studies by Lujan and colleagues[130] and Puzziferri and colleagues.[113,114]

Quality of life and comorbidities
The one- to six-month QoL outcomes for Puzziferri and colleagues[113] have been tabulated and discussed previously,[15] and can be seen in Appendix 12. In brief, early differences in some components of the SF-36 score (at one month) and Moorehead–Ardelt quality of life questionnaire (MAQoL) (at three months) were no longer significant at three months or six months respectively. At the three-year follow-up there continued to be no significant difference in MAQoL scores, and there was also no significant difference in the proportion of participants with Bariatric Analysis and Reporting Outcome System (BAROS) scores of good, very good or excellent (*Table 37*).

Westling and Gustavsson[131] reported that 92% of all patients described themselves as 'very satisfied' with the result of the operation after one year, while the remaining patients described themselves as 'satisfied'. The authors report no significant difference between the groups, but data were not provided.

Only one study reported on comorbidities.[114] At the three-year follow-up the improvement of obesity-related comorbidities was significantly different between the two groups for only two of the reported comorbidities: osteoarthritis symptoms improved more in the laparoscopic gastric bypass group than the open gastric bypass group ($p < 0.05$), whereas the open gastric bypass group experienced a greater improvement of dyslipidaemia ($p < 0.01$). For other obesity-related comorbidities improvements were not statistically significantly different between the groups (*Table 38*).

Complications and additional operative procedures
One postoperative death in the laparoscopic gastric bypass group was reported by Westling and Gustavsson;[131] this was the result of malignant hyperthermia which developed during surgery leading to the death of the patient one week later. Lujan and colleagues[130] reported three postoperative deaths. Two occurred in the laparoscopic group, one on postoperative day 32,

TABLE 36 *Summary of results: open versus laparoscopic surgery – weight change*

Open versus laparoscopic gastric bypass			
Puzziferri, 2006[113,114]	*Open RYGBP (n = 76)*	*LRYGBP (n = 79)*	*p-value*
% excess body weight loss 12 months	62 ($\pm$ 14) (*n* = 25)	68 ($\pm$ 15) (*n* = 29)	*p* = 0.07
% excess body weight loss 3 years	67 ($\pm$ 21) (*n* = 33)	77 ($\pm$ 22) (*n* = 30)	*p* = ns
% excess body weight lost 4 years	71 ($\pm$ 25) (*n* = 18)	76 ($\pm$ 19) (*n* = 22)	*p* = ns
Westling and Gustavsson, 2001[131]	*Open RYGBP (n = 21)*	*LRYGBP (n = 30)*	
BMI 1 year	30.6 ($\pm$ 4)	27 ($\pm$ 4)	
Change in BMI 1 year	13 ($\pm$ 3)	14 ($\pm$ 3)	*p* = ns
Lujan, 2004[130]	*Open GBP (n = 51)*	*LGBP (n = 53)*	
BMI 12 months (estimated from figure)	37	33	*p* = ns
BMI 18 months (estimated from figure)	36	31	*p* = ns
BMI 24 months (estimated from figure)	35	32	*p* = ns
BMI 36 months (estimated from figure)	35.5	31	*p* = ns
Sundbom, 2004[112]	*Open RYGBP (n = 25)*	*Hand-LRYGBP (n = 25)*	
Weight reduction at 1 year, median (range)	41 kg (26–57)	39 kg (23–57)	
BMI at 1 year, median	30	29	
Reduction in BMI	15	15	
Open versus laparoscopic vertical banded gastroplasty			
Davila-Cervantes, 2002[111]	*Open VBG (n = 14)*	*LVBG (n = 16)*	*p-value*
Excess body weight loss at 12 months	55% (30–88)	47% (22–97)	
BMI at 12 months, median (estimated from figure)	33	33	
Open versus laparoscopic adjustable silicone gastric banding			
de Wit, 1999[132]	Open AGB (n = 25)	LAGB (n = 25)	p-value
Mean weight loss (12 months)	34.4 kg	35 kg	*p* = ns
BMI reduction (12 months)	10.6	11.6	*p* = ns

AGB, adjustable gastric banding; BMI, body mass index; GBP, gastric bypass; hand-LRYGBP, hand-assisted laparoscopic Roux-en-Y gastric bypass; LAGB, aparoscopic adjustable gastric banding; LGBP, laparoscopic gastric bypass; LRYGBP, laparoscopic Roux-en-Y gastric bypass; LVBG, laparoscopic vertical banded gastroplasty; ns, not statistically significant; open, open surgery; RYGBP, Roux-en-Y gastric bypass; VBG, vertical banded gastroplasty.
All mean $\pm$ SD unless stated.

and the other (unrelated to surgery) six months after surgery. One death occurred in the open surgery group within the first 30 postoperative days. No postoperative deaths occurred in the open versus laparoscopic[113,114] or open versus hand-assisted laparoscopic[112] gastric bypass studies (*Table 39*).

Conversion from laparoscopy to open procedure occurred in 2.5%,[113] 8% (all in the first 20 patients),[130] and 23% of patients.[131] None of the patients with hand-assisted laparoscopy required conversion.[112] Reoperation was required in 4%,[112] 7.6%[113] and 20%[131] of laparoscopy patients, and none[112] to 6.6%[113] of patients with open gastric bypass.

In two of the studies, operative time was longer for laparoscopy [225 minutes (SD 40)[113] to 245 minutes (range 135–190)[131]] than open gastric bypass (100 minutes (range 70–150)[131] to 195 minutes (SD 41), *p* < 0.001[113]]. This was also the case for hand-

TABLE 37 *Summary of results: open versus laparoscopic surgery – quality of life*

Open versus laparoscopic gastric bypass			
Puzziferri, 2006[114]	*Open RYGBP (n = 22)*	*LRYGBP (n = 22)*	*p-value*
MAQoL scores 3 years			
Self-esteem	0.88	0.89	p = ns
Physical activity	0.36	0.40	p = ns
Social life	0.33	0.34	p = ns
Labour or work conditions	0.25	0.33	p = ns
Sexual interest/activity	0.24	0.20	p = ns
BAROS scores (%) 3 years			
Fair	9.1%	4.5%	
Good, very good or excellent	86.4%	95.5%	p = ns

BAROS, Bariatric Analysis and Reporting Outcome System; LRYGBP, laparoscopic Roux-en-Y gastric bypass; MAQoL, Moore-Ardelt Quality of Life; open, open surgery; RYGBP, Roux-en-Y gastric bypass.

assisted laparoscopy[112] (150 minutes, 110–265; open 85 minutes, 60–150, $p < 0.01$]. However, Lujan and colleagues[130] found operative time was longer for open (201.7 minutes, 129–310) than for laparoscopic gastric bypass (186.4 minutes, 125–290), $p < 0.05$.

Puzziferri and colleagues[113] found significantly less blood loss with laparoscopy (137 ml, SD 79 versus 395 ml, SD 284, $p < 0.001$), whereas Westling and Gustavsson[131] found only a slight reduction in blood loss [250 ml (50–1500) versus 300 ml (200–500), p = ns), and Sundbom and Gustavsson[112] found no difference between hand-assisted laparoscopy [median 250 ml, (0–1300)] and open surgery [median 250 ml (0–900)].

When excluding patients who were converted to open procedures, Westling and Gustavsson[131] found significant reductions in postoperative pain indicated by morphine dose, hospital stay and sick leave with laparoscopy, although the observations were not significant when using ITT analysis. Similarly, Sundbom and Gustavsson[112] found no difference in the median LOS between open and hand-assisted laparoscopic gastric bypass [open six days (range 3–7), laparoscopy six days (range 4–14)], and the amount of morphine required during the first three days was similar for the two procedures. Total sick leave was slightly higher following open surgery [hand-assisted laparoscopy 30 days (15–59), open 37 days (19–95)]. Puzziferri and colleagues,[113] however, found significant reductions in the proportion requiring intensive-care unit (ITU) stay (7.6% versus 21.1%, $p = 0.03$),

median LOS {three days [inter quartile range, (IQR), 1] versus four days (IQR 2), $p < 0.001$}, days to return to activities of daily living [8.4 days (SD 8.6) versus 17.7 days (SD 19.1), $p < 0.001$], and days to return to work [32.2 days (SD 19.8) versus 46.1 days (SD 20.6), $p = 0.02$] following laparoscopy. Lujan and colleagues[130] also found a shorter mean hospital stay following laparoscopy [5.2 days (1–13) versus 7.9 days (2–28), $p < 0.05$].

The reporting of complications varied between studies, but in all studies most complications affected a small proportion of patients. Early major complications reported by Puzziferri and colleagues[113] occurred in 9.2% of open gastric bypass patients and 7.6% of laparoscopy patients ($p = 0.78$). The most common complication in the laparoscopic group was jejunojejunostomy obstruction (3.8%) with other patients experiencing either an anastomotic leak (1.3%), hypopharyngeal perforation (1.3%), or gastrointestinal bleeding (1.3%). Participants receiving open surgery experienced wound infection (2.6%), anastomotic leak (1.3%), gastric pouch outlet obstruction (1.3%), pulmonary embolism (1.3%), respiratory failure and a retained laparotomy sponge (1.3%). Early minor complications, were similar following the open procedure (11.8% versus 7.6%, $p = 0.42$), although minor wound infections were more common following the open procedure (six patients versus one patient). Late complications were also similar (open: 15.8% versus laparoscopic: 18.9%, $p = 0.52$). Among the late complications reported by Puzziferri and colleagues[113] anastomotic stricture occurred more often after laparoscopic gastric

TABLE 38 *Summary of results: open versus laparoscopic surgery – comorbidities*

Open versus laparoscopic gastric bypass			
Puzziferri, 2006[114]	*Open RYGBP (n = 57)*	*LRYGBP (n = 59)*	
Osteoarthritis			
Baseline	31 (54%)	30 (51%)	*p* = ns
Improvement/resolution at 3 years	19 (61%)	24 (80%)	*p* < 0.05
Hypertension			
Baseline	28 (49%)	18 (31%)	*p* = ns
Improvement/resolution at 3 years	28 (100%)	15 (83%)	*p* = ns
Depression			
Baseline	17 (30%)	17 (29%)	*p* = ns
Improvement/resolution at 3 years	12 (71%)	13 (76%)	*p* = ns
Gastro-oesophageal reflux			
Baseline	21 (37%)	14 (24%)	*p* = ns
Improvement/resolution at 3 years	21 (100%)	14 (100%)	*p* = ns
Dyslipidaemia			
Baseline	14 (25%)	8 (14%)	*p* = ns
Improvement/resolution at 3 years	14 (100%)	7 (88%)	*p* < 0.01
Sleep apnoea			
Baseline	15 (26%)	5 (8%)	*p* < 0.05
Improvement/resolution at 3 years	12 (86%)	5 (100%)	*p* = ns
Diabetes mellitus			
Baseline	8 (14%)	5 (8%)	*p* = ns
Improvement/resolution at 3 years	7 (88%)	5 (100%)	*p* = ns
Infertility			
Baseline	5 (9%)	7 (12%)	*p* = ns
Improvement/resolution at 3 years	2 (40%)	2 (29%)	*p* = ns
Urinary incontinence			
Baseline	4 (7%)	8 (14%)	*p* = ns
Improvement/resolution at 3 years	4 (100%)	7 (88%)	*p* = ns
Lower extremity oedema			
Baseline	3 (5%)	2 (3%)	*p* = ns
Improvement/resolution at 3 years	3 (100%)	1 (50%)	*p* = ns

LRYGBP, laparoscopic Roux-en-Y gastric bypass; ns, not statistically significant; open, open surgery; RYGBP, Roux-en-Y gastric bypass.

bypass than open surgery but the difference was not statistically significant (laparoscopy 8.9% versus open 2.4%, *p* = 0.06), whereas ventral hernia was statistically significantly more frequent in the open surgical group (laparoscopy 0%, open 7.9%, *p* = 0.01). The difference in occurrence of hernias was still apparent at the three-year follow-up, which reports statistically significantly more patients in the open gastric banding group developed an incisional hernia than in the laparoscopic gastric banding group [22 (39%) versus 3 (5%), *p* < 0.001]. In addition, significantly more participants in the laparoscopic group required a cholecystectomy [12/43 (28%) versus 2/40 (5%), *p* = 0.03]. At three years the late complication of incisional hernia was still statistically significantly more frequent in the open surgical group (laparoscopy 5%, open 39%, *p* < 0.01), but there were no significant differences in the other complications reported at three years, and there were no late deaths (*Table 39*).

TABLE 39 *Summary of results: open versus laparoscopic surgery – complications and additional procedures*

Open versus laparoscopic gastric bypass			
Puzziferri, 2006[113,114]	*Open RYGBP (n = 76)*	*LRYGBP (n = 79)*	*p-value*
Perioperative deaths	0	0	
Late deaths	0	0	
Conversion from LGBP to GBP	n/a	2.5%	
Operative time (minutes)	195 (± 41)	225 (± 40)	*p* < 0.001
Estimated blood loss (ml)	395 (± 284)	137 (± 79)	*p* < 0.001
Intraoperative transfusion	3.9%	0	
Proportion requiring intensive-care unit stay	21.1%	7.6%	*p* = 0.03
Median length of hospital stay (days)	4 (IQR 2)	3 (IQR 1)	*p* < 0.001
Reoperation	6.6%	7.6%	*p* = ns
Return to activities of daily living (days)	17.7 (± 19.1)	8.4 (± 8.6)	*p* < 0.001
Return to work (days)	46.1 (± 20.6)	32.2 (± 19.8)	*p* = 0.02
Early major complications (total)	9.2%	7.6%	*p* = 0.78
Anastomotic leak	1	1	
Gastric pouch outlet obstruction	1	0	
Hypopharyngeal perforation	0	1	
Jejunojejunostomy obstruction	0	3	
Pulmonary embolism	1	0	
Respiratory failure	1	0	
Gastrointestinal bleeding	0	1	
Wound infection	2	0	
Retained laparotomy sponge	1	0	
Early minor complications (total)	11.8%	7.6%	*p* = 0.42
Ileus	0	1	
Clostridium difficile colitis	0	1	
Gastrogastric fistula	1	0	
Leak (asymptomatic)	1	0	
Gastrointestinal bleeding	0	2	
Wound infection	6	1	
Deep venous thrombosis	1	1	
Late complications (total)[113]	15.8%	18.9%	*p* = 0.52
Anastomotic stricture	2	9	*p* = 0.06
Prolonged nausea vomiting	2	1	
Small bowel obstruction	0	1	
Cholelithiasis	0	3	
Ventral hernia	6	0	*p* = 0.01
Anaemia	2	0	
Protein-calorie malnutrition	0	1	
Late complications at 3 years[114]	Open RYGBP (n = 57)	LRYGBP (n = 59)	
Incisional hernia	22 (39%)	3 (5%)	*p* < 0.01
Anaemia	3 (5%)	8 (14%)	*p* = ns

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TABLE 39 *Summary of results: open versus laparoscopic surgery – complications and additional procedures (continued)*

Vitamin B$_{12}$ deficiency	6 (11%)	3 (5%)	p = ns
Chronic nausea vomiting	2 (4%)	3 (5%)	p = ns
Chronic abdominal pain	1 (2%)	2 (3%)	p = ns
Marginal ulcer	1 (2%)	0	p = ns
Small bowel obstruction	1 (2%)	2 (3%)	p = ns
Cholecystectomy (excludes those with previous Cholecystectomy)	2/40 (5%)	12/43 (28%)	p = ns
Late deaths	0	0	p = 0.03
Westling and Gustavsson, 2001[131]	*Open RYGBP (n = 21)*	*LRYGBP (n = 30)*	
Deaths		1/30 (3%)	
Conversions to open surgery	n/a	7/30 (23%)	
Duration (minutes), median (range)	100 (70–150) (n = 21)	245 (135–390) (n = 30)	
Preoperative bleeding (ml), median (range)	300 (200–500) (n = 21)	250 (50–1500) (n = 30)	
Pain – morphine dose (mg)	140 (± 90) (n = 21)	98 (± 71.5) (n = 29); conversions excluded 69 (± 46.4) (n = 22)	(p = ns); p < 0.005
Hospital stay (days)	6 (± 3.8) (n = 21)	4.5 (± 1.2) (n = 29); conversions excluded 4 (± 0.8) (n = 22)	p = ns; p = 0.025
Sick leave (weeks)	5 (± 3.3) (n = 14)	3.9 (± 2.1) (n = 24); conversions excluded 2.8 (± 1.8) (n = 18)	p = ns; p = 0.025
Reoperations	1/21 (4.8%)[a]	6/30 (20%)[b]	
Gastrointestinal symptoms (dumping, vomiting, diarrhoea)	5% of all patients		
Complications (n)			
Incisional hernia		1	
Small embolus		1	
Colicky pain and vomiting		6[b]	
Leakage	1[a]		
Jejunal ulcers	2	3	p = ns
Stricture in gastrojejunostomy		1	
Superficial wound infection	3		
Readmission	1/21 (4.8%)	3/30 (10%)	
Unexplained fever	1		
Pneumonia		1	
Epigastric pain and/or vomiting		2	
Lujan, 2004[130]	*Open GBP (n = 51)*	*LGBP (n = 53)*	
Postoperative mortality	1/51 (2%)	2 (3.8%)(1 unrelated to surgery)	
Conversions to laparotomy	n/a	4/53 (8%)	
Intraoperative complications	4/51 (8%)		
Splenectomies	3		
Splenic vein tear requiring suture	1		

TABLE 39 *Summary of results: open versus laparoscopic surgery – complications and additional procedures (continued)*

Mean operating time, minutes	201.7 (129–310)	186.4 (125–290)	$p < 0.05$
Mean hospital stay, days	7.9 (2–28)	5.2 (1–13)	$p < 0.05$
Early complications (< 30 days)	15 (29.4%)	12 (22.6%)	$p = $ ns
Intestinal subocclusions	3		
Asymptomatic leaks	2		
Intra-abdominal bleeding	2		
Upper gastrointestinal haemorrhage	2	3	
Lower gastrointestinal haemorrhage	1		
Thrombophlebitis	1		
Stenosis of gastro-entero-anastomosis	1		
Subphrenic abscess		4	
Wound infection		4	
Respiratory infection		3	
Evisceration[c]		1	
Late complications (> 30 days)	12 (24%)	6 (11%)	$p < 0.05$
Intestinal obstruction[c]	3 (1 reoperation)	1 (reoperation)	
Pancreatitis/cholecystectomy	2		
Sudden death (possible pulmonary thromboembolism)	1		
Eventration		10	
Subphrenic abscess		1	
Sundbom, 2004[112]	*Open RYGBP (n = 25)*	*Hand-LRYGP (n = 25)*	
Deaths within 30 days postoperative	0	0	
Laparoscopic conversions to laparotomy	n/a	0	
Duration of surgery, minutes [Median (range)]	85 (60–150)	150 (110–265)	$p < 0.001$
Peroperative bleeding, ml [Median (range)]	250 (0–900)	250 (0–1300)	
Intra-abdominal bleeding (oozing)		3	
Intense intraluminal bleeding	2		
Patients requiring blood transfusion due to post operative anaemia	1 (2 units)	1 (2 units)	
Patients with postoperative respiratory symptoms requiring prolonged antibiotic treatment and physiotherapy treatment	5	8	
Postoperative deep venous thrombosis, pulmonary embolism, or wound dehiscence	0	0	
Length of hospital stay, days [Median (range)]	6 (3–7)	6 (4–14)	
Morphine requirement, mg:			
Day 1 [Median (range)]	32 (6–150) (n = 25)	48 (12–148) (n = 25)	
Day 2 [Median (range)]	30 (12–118) (n = 22)	36 (14–123) (n = 20)	
Day 3 [Median (range)]	25 (10–62) (n = 11)	28 (12–99) (n = 16)	
Total days 1–3 [Median (range)]	66 (6–318)	98 (12–370)	
Reoperation	0	1/25 (4%)	

TABLE 39 *Summary of results: open versus laparoscopic surgery – complications and additional procedures (continued)*

Complications at 1 month follow-up, (*n*)			
Dysphagia (various grades)		18 (group not stated)	
Narrow anastomosis	4	2	
Wound infection with pus	0	1	
Abnormal secretions		4 (group not stated)	
Total sick leave, days, median (range). (10 patients retired or on long-term sick leave excluded)	37 (19–95)	30 (15–59)	
Complications at 1-year follow-up, (*n*)			
Anaemia requiring intensive treatment		2 (group not stated)	
Symptomatic incisional hernia	1	0	
Short-term treatment with proton pump inhibitor	3	3	
Small stomal ulcer	1	0	
Open versus laparoscopic vertical banded gastroplasty			
Davila-Cervantes, 2002[111]	*Open VBG (n = 14)*	*LVBG (n = 16)*	*p-value*
Surgical details (median, min-max)			
Surgical time	1.45 hours (1.1–2.5)	2.1 hours (1.5–4.0)	$p < 0.002$
Blood transfusions	0	0	
Conversion to open surgery	n/a	0	
Hospitalisation[d]	4 days (3–42)	4 days (3–97)	p = ns
Complications (number of patients)			
Wound problems (seroma, dehiscence or infection)	6	1	
Pulmonary atelectasis requiring physical therapy		1	
Number of extra doses of analgesics: (median, min.–max.)			
1st postoperative day	2 (0–3)	1 (0–2)	p = 0.04
2nd postoperative day	1 (0–1)	2 (0–2)	p = 0.78
3rd postoperative day	1 (0–1)	0 (0)	p = 0.46
12 months follow-up			
Number with pathological scar[e]	12	5	p = 0.002
Developed abdominal wall hernias	2	0	
Open versus laparoscopic adjustable silicone gastric banding			
de Wit, 1999[132]	*Open AGB (n = 25)*	*LAGB (n = 25)*	
Conversions		Lap to open procedure: 8%	
Surgical time	76 minutes (SD 20)	150 minutes (SD 48)	$p < 0.05$
Mean days in hospital	7.2 (range 5–13)	5.9 (range 4–10)	$p < 0.05$
Early postoperative complications (lap vs open)			
Cholecystectomy	5/25 (20%)	2/25 (8%)	
Adhesiolysis		1/25 (4%)	
Gall bladder puncture (to obtain samples for study purposes)	7/25 (28%)	0	
Pulmonary complications	2/25 (8%)	2/25 (8%)	

TABLE 39 *Summary of results: open versus laparoscopic surgery – complications and additional procedures (continued)*

Urinary infection	0	2/25 (8%)	
Rhabdomyolysis	0	1/25 (4%)	
Neurological complication (neuropraxis)	1/25 (4%)	1/25 (4%)	
Perforation pouch	1/25 (4%)	0	
Wound abscess	1/25 (4%)	0	
Fever	2/25 (8%)	0	
Gout	1/25 (4%)	0	
First year surgical complications			
Incisional hernia	7 (28%), in 3 (12%) patients	0	p = ns
Migration band	1/24 (4%)	0	p = ns
Umbilical hernia	0%,	1/25 (4%)	p = ns
Access port complications	6 (24%) in 5 (20%) patients	7 (28%), in 5 (20%) patients	p = ns
Readmissions			
Patients	7/24 (28%)	5/25 (20%)	p = ns
Total readmissions	15/24	6/25	$p < 0.05$
Overall length of hospital stay in the first year, days	11.8 (SD 10.5)	7.8 (SD 6)	$p < 0.05$

AGB, adjustable gastric banding; GBP, gastric bypass; hand-LRYGBP, hand-assisted laparoscopic Roux-en-Y gastric bypass; IQR, inter quartile range; LAGB, laparoscopic adjustable gastric banding; LGBP, laparoscopic gastric bypass; LRYGBP, laparoscopic Roux-en-Y gastric bypass; LVBG, laparoscopic vertical banded gastroplasty; n/a, not applicable; n/s, not statistically significant; open, open surgery; RYGBP, Roux-en-Y gastric bypass; SD, standard deviation; VBG, vertical banded gastroplasty.
All mean (± SD) unless stated.
a The patient in the open surgery group who required reoperation was the only patient with an obvious leakage.
b Six patients were reoperated on: five due to narrow stricture of the tunnel through the mesocolon and one due to a herniated Roux limb.
c This complication led to one patient death.
d One patient in each group developed fistula at gastric partition requiring reoperation and prolonged hospital stay.
e Pathological scar is a term used to describe particular types of abnormal/severe scar.

In contrast to Puzziferri and colleagues,[113] Lujan and colleagues[130] reported four intraoperative complications in the open gastric bypass group and none in the laparoscopic group. They also found that while there was no significant difference between early complications (laparoscopy 22.6%, open 29.4%), late complications (> 30 days) were more common following open gastric bypass (11% versus 24%, $p < 0.05$). The most common early complications for laparoscopy included intestinal subocclusions (5.7%), asymptomatic leaks (3.8%), intra-abdominal bleeding (3.8%) and upper gastrointestinal haemorrhage (3.8%). For open surgery these included subphrenic abscesses (7.8%), wound infections (7.8%), upper gastrointestinal haemorrhage (5.9%) and respiratory infection (5.9%). The most common late complications reported by Lujan and colleagues[130] included intestinal obstructions (5.7% of laparoscopy patients) and eventrations

(protrusion of intestines through wound) (19.6% of open surgery patients). Late complications led to two reoperations, one in each group. Sundbom and Gustavsson[112] reported that postoperative respiratory symptoms requiring prolonged antibiotic treatment and physiotherapy treatment occurred in 32% of hand-assisted laparoscopy patients and 20% of open surgery patients. Other complications included various grades of dysphagia (36% of patients, group not stated), narrow anastomosis (hand-assisted laparoscopy 8%, open 16%), and short-term treatment with a proton pump inhibitor (12% of each group). Westling and Gustavsson[131] did not report early and late postoperative complications separately. The most commonly reported complications occurring after surgery were reoperations (discussed earlier), most often as the result of stricture of the tunnel through the mesocolon causing colicky pain and vomiting, jejunal ulcers (laparoscopy 10.3%, open

9.5%), and superficial wound infection (open 14.3%). There were four readmissions in the first year (laparoscopy 10.3%, open 4.7%) and one participant (4.7%) who had received open surgery developed an incisional hernia (*Table 39*).

Gastrointestinal symptoms reported at one year, such as dumping, vomiting or diarrhoea, were experienced by 5% of all patients in Westling and Gustavsson.[131]

Summary
Four trials were included. The risk of selection bias was high in one trial, low in one trial and uncertain in two trials, and the risk of bias from other sources was mostly uncertain as many factors were not reported. Weight loss and QoL were similar between open and laparoscopic gastric bypass. Only one study reported on comorbidities and improvements were similar between the procedures except for two of the comorbidities. Statistically significant differences were found in favour of laparoscopic gastric bypass for a number of operative characteristics, particularly hospital stay in some studies. Complications in the two groups were in general reported to be not significantly different or were reported without a statistical comparison having been made.

Open versus laparoscopic vertical banded gastroplasty
One RCT compared open vertical banded gastroplasty with laparoscopic vertical banded gastroplasty.[129]

Weight change
Davila-Cervantes and colleagues[111] reported similar excess weight loss at 12 months (open 55% versus laparoscopic 47%, statistical significance not reported), resulting in a median BMI of 33 in both groups. In addition data were presented by the trial authors as median and range so care should be taken when interpreting the results (*Table 36*).

Quality of life and comorbidities
Data on QoL or comorbidities were not assessed. The median patient satisfaction score at 12 months was higher among the patients undergoing laparoscopic surgery [median score 2 (0–2) versus 1 (0–2), $p = 0.006$].

Complications and additional operative procedures
There were no conversions from laparoscopic to open surgery. Surgical time was longer with laparoscopy [median 2.1 hours (1.5–4.0) versus 1.45 hours (1.1–2.5), $p < 0.002$], but there was no

statistically significant difference in LOS (median four days in both groups). Patients undergoing open surgery required more extra doses of analgesics on the first postoperative day [open median 2 (0–3), laparoscopic median 1 (0–2), $p = 0.04$], but not the second or third day. Wound problems such as seroma (accumulation of fluid), dehiscence (opening of wound) or infection were experienced by 43% of the open surgery group, whereas 6% of the laparoscopy group experienced wound infection and 6% experienced pulmonary atelectasis requiring physical therapy. One patient in each group developed a fistula at the gastric partition which required reoperation and prolonged hospital stay. Fewer laparoscopic patients had a pathologic scar at 12 months (five patients versus 12 patients, $p = 0.002$). Two patients (14%) with open surgery developed abdominal wall hernias (*Table 39*).

Summary
Similar excess weight loss occurred following open and laparoscopic vertical banded gastroplasty and LOS was not significantly different between the two groups. Operative time was statistically significantly shorter for the open surgery group but after surgery fewer laparoscopic patients had wound problems and at 12 months fewer had a pathological scar. Laparoscopic patients had a higher patient satisfaction score at 12 months. This small RCT has an uncertain risk of bias as many factors were not reported.

Open versus laparoscopic adjustable silicone gastric banding
One RCT compared open adjustable silicone gastric banding with laparoscopic adjustable silicone gastric banding.[132]

Weight change
De Wit and colleagues[132] demonstrated no significant difference in weight loss between the procedures 12 months after surgery ($p = $ ns). However, both laparoscopic and open adjustable silicone gastric banding were associated with a significant reduction in weight compared with baseline (35 kg and 34.4 kg respectively, $p < 0.05$) (*Table 36*).

Quality of life and comorbidities
Data on QoL or comorbidities were not assessed.

Complications and additional operative procedures
Surgical complications and access port complications did not differ significantly between the two procedures, although patients undergoing

the open procedure had higher proportions of incisional hernia complications compared with laparoscopy (12% versus 0%, p = ns). Similarly early postoperative complications differed little between open and laparoscopic adjustable silicone gastric banding, although there were greater proportions of cholecystectomy among those undergoing open procedures (20% versus 8%). Readmissions (15 among 7/24 open patients versus six among 5/25 laparoscopic surgical patients, $p < 0.05$) following open and laparoscopic surgery, respectively, and mean overall LOS in the first year (11.8 days versus 7.8 days, $p < 0.05$) were significantly higher in those undergoing open compared to laparoscopic procedures (*Table 39*).

Two (8%) patients were converted from laparoscopic to open procedure because of an inability to obtain a pneumoperitoneum. Laparoscopic surgery was rated as more difficult than open surgery ($p < 0.05$), and took longer to perform [150 minutes (SD 48) versus 76 minutes (SD 20), $p < 0.05$] (*Table 39*). Difficulty of surgery was rated on a subjective scale from 1 = easy to 10 = could not be performed or had to be converted, and therefore the finding should be treated with some caution.

Summary

Open and laparoscopic surgeries to fit adjustable silicone gastric banding led to similar degrees of significant weight loss. Operative time was statistically significantly shorter for the open surgery group. However, participants undergoing open procedures had a significantly longer hospital stay and were significantly more likely to be readmitted to hospital. Early postoperative complications were similar between the groups, but incisional hernia complications were experienced by 12% of patients who received the open procedure and by none of the laparoscopic surgical group. This study had a low risk of selection bias and a low risk of bias from incomplete weight loss data.

Summary of clinical effectiveness

Many of the included RCTs had an uncertain risk of bias because the reporting was unclear. Just five RCTs reported adequate allocation concealment and were, therefore, at low risk of selection bias. Most studies did not mention whether outcomes assessors were blinded to intervention assignments. The reporting of incomplete outcome data for weight loss, QoL or comorbidity was unclear for almost half of the studies. Other sources of bias included the use of block randomisation in non-blinded trials, making it possible to predict future assignments. The included cohort studies were of variable size and quality. Most study participants were women so it is uncertain how generalisable the results are to men. All the studies included in this review were conducted in countries other than the UK. It is difficult to determine how generalisable the results of the included studies are to the ethnically diverse population within the UK.

Clinical effectiveness of surgery versus non-surgical interventions

Three RCTs and three cohort studies contributed evidence on the comparison of surgical versus non-surgical interventions for obesity. All the studies reported that surgery results in greater weight loss than a non-surgical weight loss intervention even though they varied in the types of surgery undertaken, the non-surgical comparator, and the participants included. Two RCTs focused on participants at the lower side of the obesity continuum, one was judged to have a high risk of selection bias, and the other a low risk of selection bias, but at an uncertain risk of other sources of bias. These trials reported mean percentage excess weight loss at two years of 62.5% and 87.2% following surgery, but only 4.3% and 21.8% excess weight loss in participants in the non-surgical groups of these trials. The third RCT, judged to have an uncertain risk of bias, focused on people with morbid obesity, but again weight loss in men and women participants was greater one year following surgery (35 kg and 52 kg) than following diet (7 kg and 9 kg). Bias is inherently more likely within cohort studies than RCTs for a variety of reasons, but chiefly because there is a risk that confounding factors (both known and unknown) are distributed unevenly between the cohorts and the lack of randomisation provides an opportunity for selection bias to take place. The possible effect of these biases must therefore be kept in mind when interpreting the results of such studies. As noted above all the included cohort studies reported greater weight loss following surgical intervention than a non-surgical alternative. One of the three cohort studies, the large SOS study, has also reported the longest follow-up of all the included studies and therefore provides some evidence for the maintenance of the difference in weight loss for as long as 10 years.

Quality of life characteristics were reported by one of the RCTs and two of the cohort studies. The RCT provided evidence for an improvement

in some aspects of QoL at two years in patients who had undergone surgery, whereas one of the cohort studies found that after 3.2 years there were no significant differences between the groups. In contrast the larger SOS cohort study reported that all HRQoL measures were improved at 10 years compared with baseline for the surgery group, but for the conventional group some had improved while others had worsened.

One of the RCTs focused on participants at the lower side of the obesity continuum who also had Type 2 diabetes. In this study, remission of Type 2 diabetes at two years was significantly higher in the surgery group than in the conventional therapy group and surgically treated participants were less likely to have metabolic syndrome. The other RCT focusing on participants at the lower end of the obesity continuum also reported a statistically significant reduction in the proportion of surgically treated participants with metabolic syndrome at two years. The SOS cohort study again provides evidence that improvements in comorbidities such as Type 2 diabetes and metabolic syndrome can be maintained at least for 10 years. Another weight-related comorbidity, hypertension, was improved in one of the RCTs at two years and in the SOS study at 10 years, but the difference was not statistically significant at these time points.

Two of the RCTs reported that there were adverse events associated with both surgical and non-surgical interventions and the SOS cohort study reported on complications and adverse events for the surgical group only, as well as overall mortality for both groups. The SOS study reported five deaths (0.25%) within 90 days of surgery in the surgical group in comparison with two deaths (0.10%) that occurred during the same period in the non-surgical group. During long-term follow-up (of mean duration 10.9 years) 5% of the surgical group died in comparison with 6.3% of the non-surgical group.

Clinical effectiveness of different surgical interventions

The clinical effectiveness of different surgical interventions was assessed by 20 RCTs which between them focused on nine different comparisons: six comparisons of different types of bariatric surgery and three comparisons of open and laparoscopic approaches to bariatric surgery. Among the six comparisons of different types of bariatric surgery there were three comparisons of procedures combining restrictive

and malabsorption components with restrictive procedures (gastric bypass versus vertical banded gastroplasty; gastric bypass versus adjustable gastric band, and gastric bypass versus laparoscopic sleeve gastrectomy), two comparisons between restrictive procedures (vertical banded gastroplasty versus adjustable gastric band, and adjustable gastric band versus laparoscopic isolated sleeve gastrectomy), and one comparison between unbanded gastric bypass and banded gastric bypass.

Four comparisons included gastric bypass compared with either vertical banded gastroplasty (seven RCTs), banded gastric bypass (one RCT), adjustable gastric banding (one RCT), or laparoscopic sleeve gastrectomy (one RCT). On measures of weight change gastric bypass, which combines restrictive and malabsorption components, was superior to the purely restrictive procedures of vertical banded gastroplasty, and laparoscopic adjustable gastric banding. The comparison with laparoscopic sleeve gastrectomy was inconclusive. For people with a BMI over 50, banded gastric bypass was similar to non-banded gastric bypass.

The comparisons between restrictive procedures included three RCTs which contributed evidence on the comparison between vertical banded gastroplasty and adjustable gastric banding, and the results were inconclusive. All studies found greater initial weight loss following vertical banded gastroplasty, but one study found no statistically significant difference at two or three years follow-up, one study found that vertical banded gastroplasty patients regained weight, so that at three to five years follow-up weight loss was greater following adjustable gastric banding (statistical significance not reported), and one study found that per cent excess BMI loss was greater with vertical banded gastroplasty at the seven-year follow-up (statistical significance not reported). The final comparison of different types of bariatric surgery, laparoscopic adjustable gastric banding versus laparoscopic isolated sleeve gastrectomy (both restrictive procedures) was assessed by only one RCT that reported weight-related outcomes at one and three years. All the data were reported as median and range and at both time points the participants who had received isolated sleeve gastrectomy showed more improvement than participants who had received adjustable gastric banding.

The comparisons of open versus laparoscopic gastric bypass (four RCTs), open versus

laparoscopic vertical banded gastroplasty (one RCT), and open versus laparoscopic adjustable silicone gastric banding (one RCT) all found that there were no significant differences in weight loss outcomes between the open and laparoscopic surgical approaches, both groups lost similar amounts of weight.

Only two RCTs comparing surgical procedures assessed QoL. One RCT reported that following surgery QoL was better in the gastric bypass group than in the vertical banded gastroplasty group on some items. The other RCT assessed people who had received either open or laparoscopic gastric bypass and found that there was no significant difference between the groups in QoL measures.

Five of the 20 RCTs assessing the clinical effectiveness of different surgical interventions reported on changes in comorbidities after surgery. In general comorbidities improved in all groups with no significant differences in improvements observed between different surgical interventions.

Reporting of adverse events, complications and operative variables varied greatly between studies and statistical comparisons between the groups were not often made. In general, adverse events and complications affected few participants. Fourteen of the 20 RCTs reported no deaths during or shortly after surgery and the remaining six RCTs reported very few deaths. Where deaths were reported separately for each trial arm, mortality ranged from 2% (one death within the first 30 postoperative days among 51 patients receiving open gastric bypass surgery) to 10% (two deaths among 20 patients receiving open Roux-en-Y gastric bypass; one on the fourth postoperative day and one after 13 months).

Two studies provided evidence that laparoscopic vertical banded gastroplasty surgery is quicker, and is associated with fewer early postoperative complications than laparoscopic gastric bypass surgery. However, approximately three years following open surgery to provide a vertical banded gastroplasty, conversions to an alternative bariatric procedure occurred more often than after open gastric bypass, but neither of the two studies reporting this comparison tested the outcome for statistical significance. Complications were generally similar for banded and unbanded gastric bypass apart from emesis and food intolerance, which were statistically significantly worse in the banded gastric bypass group. Laparoscopic gastric bypass was associated with a similar level of early complications and reoperations as laparoscopic adjustable gastric banding in the one RCT that compared these procedures. A further small RCT that compared laparoscopic gastric bypass with laparoscopic sleeve gastrectomy reported no intraoperative or postoperative complications in either group. Operative time was shorter for laparoscopic adjustable gastric banding than for laparoscopic vertical banded gastroplasty and hospital stay was also shorter than for laparoscopic or open vertical banded gastroplasty. However, there were statistically significantly more late complications following laparoscopic adjustable gastric banding than laparoscopic vertical banded gastroplasty in the trial that reported this comparison. Open vertical banded gastroplasty was associated with more infections than laparoscopic adjustable gastric banding. In the RCT that compared laparoscopic isolated sleeve gastrectomy with laparoscopic adjustable gastric banding there were more early postoperative complications with laparoscopic isolated sleeve gastrectomy, but late complications were higher in the laparoscopic adjustable gastric banding group. The comparisons of open and laparoscopic procedures in general favour the laparoscopic procedure for a number of operative characteristics, particularly hospital stay, and with fewer laparoscopic patients experiencing wound problems or incisional hernia complications.

Chapter 5
Assessment of cost-effectiveness

Introduction

The aim of this section is to assess the cost-effectiveness of multiple types of surgical treatments for adults with morbid obesity (i.e. with BMI > 40), compared with non-surgical treatments, as well as a comparison of surgical treatments to each other. The cost-effectiveness of surgical treatment of obese patients (i.e. with BMI more than 35, but less than 40) with significant comorbidities is also analysed. The definition of the obese population here is consistent with the definition in the NICE Guidelines[9] and with the general criteria of eligibility for bariatric surgery, as used in the cost-effectiveness studies[138–142] presented below. The obese population here is therefore defined according to narrower criteria than those used for clinical effectiveness (see Chapter 3, Inclusion criteria).

The following types of surgical intervention treatments were included:

- open gastric bypass
- laparoscopic gastric bypass
- vertical banded gastroplasty
- laparoscopic adjustable gastric banding
- biliopancreatic diversion and duodenal switch.

Results

Results of the literature search

A total of 448 reports of studies on the economics of surgical treatments were identified from which 36 citations were retrieved as potentially eligible for inclusion and the full papers were obtained. Two systematic reviews[51,143] of economic analyses of surgical interventions and five original economic evaluations[138–142] that met the inclusion/exclusion criteria described in Chapter 3, Inclusion criteria were identified from the full reports (listed below). The reasons for excluding 29 studies after examination of the full papers can be seen in Appendix 17.

Included systematic reviews of cost-effectiveness of bariatric surgery

1. Relevant parts of Chapter 4 in the 'Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement' by Avenell and colleagues.[51]
2. 'Are bariatric surgical outcomes worth their cost? A systematic review' by Salem and colleagues.[143]

The two systematic reviews listed above were used as sources for economic evaluations published since searches were undertaken in 2001 for the previous review published in 2002.[15] The final search for economic evaluation studies in the systematic review by Avenell and colleagues[51] does not include any reports published after 2001. The systematic review by Salem and colleagues[143] identified only three publications that reported the cost-effectiveness of bariatric surgery as cost per QALY, including our previous 2002 systematic review and economic evaluation.[15] Only one of these three economic evaluation studies[140] was published after 2001. This study is included in the list below of five newly identified original economic evaluations published after 2001. In addition to this study,[140] four other original economic evaluations that met the inclusion/exclusion criteria were identified and appraised.

Original economic evaluations of bariatric surgeries included in the current review

1. Ackroyd R, Mouiel J, Chevallier JM, Daoud F. 'Cost-effectiveness and budget impact of obesity surgery in patients with type-2 diabetes in three European countries'.[138]
2. van Mastrigt GA, van Dielen FM, Severens JL, Voss GB, Greve JW. 'One-year cost-effectiveness of surgical treatment of morbid obesity: vertical banded gastroplasty versus Lap-Band'.[139]
3. Craig BM, Tseng DS. 'Cost-effectiveness of gastric bypass for severe obesity'.[140]
4. Jensen C, Flum DR. 'The costs of nonsurgical and surgical weight loss interventions: is an ounce of prevention really worth a pound of cure?'.[141]

5. Salem L, Devlin A, Sullivan SD, Flum DR. 'Cost-effectiveness analysis of laparoscopic gastric bypass, adjustable gastric banding, and nonoperative weight loss interventions'.[142]

Four of the identified studies were designed to estimate the cost-effectiveness of bariatric surgery in comparison with non-surgical treatment[138,140–142] and one study, by van Mastrigt and colleagues[139], conducted a head-to-head comparison of clinical and economic effectiveness of two surgical alternatives. The study by van Mastrigt and colleagues[139] is an economic evaluation alongside a clinical trial conducted over a one-year time interval. In this study the utility values were directly obtained from the trial participants. The four other studies are based on a decision analytic model that extrapolated the time horizon beyond the duration of clinical trials used as a source of clinical effectiveness and transformed an intermediate outcome (a body-weight reduction) into the final outcome (QALY or LY). Three out of the four modelled economic evaluations[140–142] have a lifetime horizon and one[138] has a five-year horizon.

The studies differ with respect to: characteristics of the populations included in economic models (e.g. the baseline age, BMI and presence of comorbidities); perspectives of the evaluations (i.e. of a health-care system, a payer's or a societal perspective); and, the source of clinical and epidemiological evidence. The study by van Mastrigt and colleagues[139] has been undertaken from the societal perspective (the Netherlands). The only other study conducted from the societal (the USA) perspective is Jensen and Flum.[141] This and two other studies[140–142] use the same published US clinical, epidemiological and economic data.[144] Only one study, by Ackroyd and colleagues,[138] used UK data along with data from Germany and France. These issues are further elaborated in subsequent sections.

Description of the identified studies

Table 40 shows a list of surgical and non-surgical interventions from the identified studies and maps them across the list of surgical interventions included in the economic evaluation undertaken for this report.

Table 40 shows that none of the economic evaluations involved the whole range of treatment alternatives for obesity. None of the identified studies included biliopancreatic diversion and duodenal switch, so this type of bariatric surgery was excluded from further consideration. Two studies, Craig and Tseng[140] and Jensen and Flum,[141] compared open gastric bypass with non-surgical treatment, although the definitions of non-surgical treatment differ in these two studies. Two other studies, by Ackroyd and colleagues[138] and Salem and colleagues,[142] reported pair-wise comparisons of laparoscopic gastric bypass with a no-treatment strategy and laparoscopic adjustable gastric banding with a no-treatment strategy respectively. These studies differ with respect to the population included (only patients with Type 2 diabetes were included in Ackroyd and colleagues[138]) and the health-care systems where the intervention took place. Ackroyd and colleagues[138] conducted economic evaluations using data from three European countries – the UK, Germany and France – whereas Salem and colleagues[142] used clinical, epidemiological, cost and economic outcomes data from the USA. The only study that conducted a head-to-head comparison of two alternative surgical interventions was an economic evaluation alongside a clinical trial undertaken in a single Netherlands hospital.[139]

The studies were summarised and critically appraised according to the methods described in Chapter 3, Quality assessment. The studies are characterised by large variations across the characteristics of the population, the interventions and the countries where the interventions took place so no formal quantitative systematic analysis of the results is possible. However, the strengths and weaknesses of the studies are presented in the Summary section of this chapter and the appraisal allowed us to make some judgements about the credibility of reported results and recommendations that the authors of identified studies had made.

Table 41 provides a summary of the characteristics of the five included published economic evaluations of surgical treatment alternatives for obesity (see Appendix 15 for full data extractions and critical appraisal of each study).

The target population.

The studies presented in *Table 41* are consistent with respect to the definition of the obese population for whom a surgical intervention is recommended according to NICE guidelines:[9] patients with BMI ≥40 or with BMI between 35 and 40 and with a significant disease such as Type 2 diabetes or high blood pressure. At the same time the studies differ with respect to baseline characteristics of the target population such as age

TABLE 40 *Surgical and non-surgical interventions included in the identified studies*

Study	Type of treatment strategies				
	Non-surgical treatment (description)	Open gastric bypass (Open GBP)	Laparoscopic gastric bypass (LGBP)	Open vertical banded gastroplasty (VBG)	Laparoscopic adjustable gastric banding (LAGB)
Ackroyd and colleagues[138,a]	Conventional treatment for obese Type 2 diabetes patients[b]		X		X
van Mastrigt and colleagues[139]	–			X	X
Craig and Tseng[140]	No treatment[c]	X			
Jensen and Flum[141]	Diet and exercise	X			
Salem and colleagues[142,a]	Non-operative weight loss interventions[d]		X		X

a   The studies by Ackroyd and colleagues and Salem and colleagues do not include a direct comparison between the alternative surgical interventions (contrary to the statement made in the latter). Only pair-wise comparisons of each surgery with a non-surgical intervention are reported.
b   The conventional treatment was identified as either 'annual follow-up watchful waiting' or 'continuation of the second year of a medically guided dieting' that is assumed to be undertaken in the first year.
c   It is not clear whether a 'no-treatment' comparator arm means no surgical treatment or no other interventions like dieting, exercise, behaviour therapy and pharmacotherapy. In either case a zero clinical effectiveness in terms of weight loss
d   Not elaborated, however assumed to be associated with a zero clinical effectiveness in terms of weight loss.

(ranging from 35 to 55 years old) and the presence or absence of comorbidities. Craig and Tseng[140] and Salem and colleagues[142] have assumed that the population of obese patients with BMI ≥40 have no comorbidities at baseline, which may not be a realistic assumption and would limit the generalisability of results. Likewise, the outcomes reported in Ackroyd and colleagues[138] are only applicable to the population of obese patients with Type 2 diabetes. The outcomes reported in Jensen and Flum[141] are applicable only to white female patients who were obese at the age of 18 with BMI ≥33 (or 35) (see *Table 41*, footnote d). The population enrolled in the study by van Mastrigt and colleagues[139] appears to be the closest to the population typically presented in (European) clinical practice for bariatric surgery as it consists of both male and female patients with a mix of obesity-related comorbidities.

Sources of clinical evidence for weight reduction used in the modelled economic evaluations.

Four modelled economic evaluations[138,140–142] used the primary clinical end point of reduction in BMI (or per cent excess weight loss converted into BMI values). In all four studies the BMI values were

taken from the published evidence; however, it does not appear that a systematic literature search and evidence synthesis was conducted in these studies. The economic analysis reported in Craig and Tseng[140] and Jensen and Flum[141] was based on bariatric surgery outcomes obtained from a single published source of evidence (a case series study by Pories and colleagues[148] and a case–control longitudinal study by Sjostrom and colleagues,[89] respectively). The likelihood of a biased estimate of clinical outcomes is the highest in the case of a single and/or uncontrolled clinical study, which potentially affects validity of the estimate of the differential weight loss and generalisability of the results.

Primary and secondary clinical outcome(s) used in the modelled economic evaluations.

The short-term intervention period (which is defined differently across the studies) is also characterised by the likelihood of an operative mortality and possible immediate and subsequent complications, some of which may result in surgical revisions (see Assumptions of economic evaluations, this chapter). Differential operative mortality rates (including mortality in revision and/or reversal

TABLE 41 *Characteristics of economic evaluations of surgical treatments of obesity*

Author	Ackroyd and colleagues[138]	van Mastrigt and colleagues[139]	Craig and Tseng[140]	Jensen and Flum[141]	Salem and colleagues[142]
Publication year	2006	2006	2002	2005	2008
Country	UK, Germany and France	the Netherlands	USA	USA	USA
Currency base	2005 British pound in UK analysis and 2005 Euro in German and French analyses[a]	The resources were first assessed in 1999 Netherlands guilders and then converted to euros[b]	2001 US dollars	2004 US dollars	2004 US dollars
Study type	CEA and CUA	CEA and CUA	CEA and CUA	CUA	CUA
Study perspective	The payers' perspective (i.e. NHS in the case of UK)	A societal perspective	The payers' perspective (i.e. the insurers' + patients' copayments)	A societal perspective	The payers' perspective (i.e. the insurers' + patients' copayments)
Study population (definition of obesity/ eligibility for surgery)	BMI > 35 and Type 2 diabetes. Eligible patients need to fail at least one prior year of medical treatment. The mean age of the target population is not reported	BMI > 40 or BMI between 35–40 and a significant comorbidity. VBG mean age 38.9 (SD = 8.53). LAGB mean age 37.2 (SD = 9.64)	BMI 40 to 50. Non-smoking males and females 35–55 years of age without a cardiovascular disease, who failed conservative therapies of dieting, exercise, behaviour therapy and pharmacotherapy[c]	The cohort of white female patients enter each arm of the model at the age of 18 with BMI of 33 or 35.[d] The patients in the surgical intervention arm undergo open GBP at the age of 40 and BMI ≥40	BMI of 40 to 60. Males and females 35–55 years of age without any obesity-related comorbidity at the baseline
Surgical intervention(s) and the comparator treatment	LAGB vs conventional treatment and LGBP vs Conventional treatment	Head-to-head comparison of VBG with LAGB	Open GBP vs no treatment	Open GBP vs diet and exercise	LAGB vs no treatment and LGBP vs no treatment
The primary clinical treatment effects modelled/assessed	1 kg/m² of BMI reduction (or increase) and Type 2 diabetes prevalence	Reduction in % EWL, operative mortality	Operative mortality; rates of revision surgery and reversal surgery; % EWL[e]	Mortality rates from immediate complications; BMI reduction;	Operative mortality; % EWL[e]
Source of clinical evidence for the primary effect	For LAGB the data on BMI reduction and Type 2 diabetes prevalence were taken from Clegg and colleagues;[15] NICE guidelines[9] and 13 publications including non-randomised cohort studies and case series. For LGBP the data on BMI reduction and Type 2 diabetes prevalence were extracted from 11 publications.	The clinical data were collected from 100 patients (50 in each arm) enrolled in a RCT comparing clinical and cost-effectiveness of VBG and LAGB. The clinical outcomes are reported in van Dielen and colleagues[147]	Primary source of clinical effectiveness data (BMI, mortality and complication rates) is a case series study of 608 morbidly obese patients followed up for 14 years with a 96.3% follow-up rate (Pories and colleagues[148]); Rates of reversal surgeries were taken from RCT of open GBP vs laparoscopic VBG by Hall and colleagues[149]	BMI reduction and complication rates were taken from the SOS study.[89] 346 surgical patients were matched with 346 non-surgical controls and followed up for eight years. For the comparator data on BMI reduction were taken from Heshka and colleagues.[150]	Operative mortality was taken from the systematic literature review of LAGB by Chapman and colleagues.[151] Estimates of the primary clinical end points (% EWL) were taken from the range of studies including cohort and case series studies.

Author	Ackroyd and colleagues[138]	van Mastrigt and colleagues[139]	Craig and Tseng[140]	Jensen and Flum[141]	Salem and colleagues[142]
	For the comparator the BMI reduction data and Type 2 diabetes prevalence over three years were taken from the Swedish HTA systematic review and the US Clinical guidelines[145,146] and extrapolated for the years 4 and 5 of the time horizon in the model.			211 patients undergoing a diet and exercise commercial programme were matched with 212 controls undergoing a self-help programme and followed up for two years.	
Secondary treatment effects (e.g. safety of surgical procedure)	The rates of revision and reversal surgeries and complications that do not require surgery were not included on the outcome side of the cost-effectiveness calculations, but were included on the cost side. The operative- and obesity-specific and all courses mortality was implicitly assumed to be zero.	The differential operative mortality rates were recorded.	The differential non-surgical complications were not consistently included in the ICER (i.e. the associated disutility was omitted from the outcome side of the cost-effectiveness calculations)	It is not clear how immediate complications are defined and whether mortality associated with both revision and reversal surgeries was included in the LY estimate. It does not appear that the treatment of subsequent complications (e.g. cholecystectomy and abdominoplasty) undertaken within two to five years after surgery was included in the model	The differential non-surgical complications were not consistently included in the ICER (i.e. the associated disutility was omitted from the outcome side of the cost-effectiveness calculations)
Outcomes used in CEA (if applicable)	Incremental cost per BMI × year; incremental cost per Type 2 diabetes-free year	Incremental cost per 1% of extra weight loss – EWL	Incremental cost per life-year saved	Not applicable	Not applicable
Final outcomes (i.e. QALY or LY)	QALY	QALY	LY, QALY	QALY	QALY
Discounting (and values)	Costs and QALYs were discounted at 3.5%; outcomes used in CEA were not discounted	Not applicable, the duration of the RCT and economic evaluation was one year	Cost and outcomes are discounted at 3%	Discounting of costs or outcomes seems to have been conducted but the discounting rate(s) are not reported	Cost and outcomes are discounted at 3%

BMI, body mass index; CEA, cost-effectiveness analysis; CUA, cost–utility analysis; EWL, excess weight loss; GBP, gastric bypass; ICER, incremental cost-effectiveness ratio; LAGB, laparoscopic adjustable gastric bypass; LGBP, laparoscopic gastric bypass; LY, life year; QALY, quality-adjusted life-year; RCT, randomised controlled trial; SD, standard deviation; SOS, Swedish Obese Subjects; VBG, vertical banded gastroplasty.

a   The cost of comparator treatment of obese patients with Type 2 diabetes was apparently expressed in 1998 prices (according to the source the CODE-2 data).

b   The conversion rate and a year to which it was applied was not reported.

c   The definition of the target population is inconsistent with the characteristics of the population in the trial[148] used a source of clinical effectiveness data.

d   There is a discrepancy in the reported baseline BMI.

e   BMI measure was obtained from % EWL; however, the conversion rule is not provided.

surgeries) are translated into the different life expectancy in the intervention and the comparator arms. Some patients also require reversal surgery (e.g. a band removal after laparoscopic adjustable gastric banding). The study by Jensen and Flum[141] includes only immediate (unspecified) postsurgical complications and associated mortality. The studies by Ackroyd and colleagues,[138] Craig and Tseng,[140] and Salem and colleagues[142] include a fairly complete list of both immediate and subsequent complications (e.g. cholecystectomy, abdominoplasty).

The study by Ackroyd and colleagues[138] seems to have implicitly assumed a zero mortality rate (i.e. operative mortality, all-cause mortality and mortality associated with obesity-specific comorbidities, were all assumed to be zero) in all treatment options over the entire five years of the modelled time interval. It effectively implies that the differential operative mortality in the interventions (laparoscopic adjustable gastric banding and laparoscopic gastric bypass) and the comparator arms (non-surgical treatment) do not have an effect on the estimates of LYs and QALYs. The same also applies to the differential rates of postsurgical complications, including revision and reversal surgeries. These implicit assumptions do not seem to be reasonable and may potentially affect the validity of the estimate of the LYs gained and the generalisability of the results.

All modelled economic evaluations applied a discounting rate to both costs and outcomes although Jensen and Flum[141] did not specify the value of the discounting rate.

Critical appraisal of economic evaluations

Table 42 outlines the approaches used in the identified cost-effectiveness studies. For completeness, the only economic evaluation that was not based on a decision analytic model[139] is also included.

The economic evaluation alongside a clinical trial reported by van Mastrigt and colleagues[139] and the deterministic models reported in the other studies[138,140–142] are two different methods of assessing the cost-effectiveness of bariatric surgery, and therefore cannot be directly compared across the whole range of criteria used for critical appraisal of decision analytic models.[77] Nevertheless, as reported below, some selected criteria can be used across the entire range of the identified economic evaluations.

Assumptions of economic evaluations

Time horizon

The time horizon of the economic evaluation in van Mastrigt and colleagues[139] is only one year. The authors have acknowledged the short-term horizon as one of the limitations of the study. In particular, the two types of bariatric surgery (laparoscopic adjustable gastric banding and vertical banded gastroplasty) compared in the study are characterised by the differential speed at which patients lose weight during the first 12 months. This is because the laparoscopic adjustable gastric banding patients need to undertake a few band adjustments in the first year following surgery, therefore losing weight in a more gradual fashion. The authors suggested that it is reasonable to expect that the patients in the laparoscopic adjustable gastric banding arm will continue to lose weight in the following postoperative years (up to five years), while the weight loss trend in the vertical banded gastroplasty arm will reach a plateau or even reverse after the first year.[126]

The five-year time interval, as opposed to one year, was recommended in Clegg and colleagues[15] as appropriate for assessing the (short-term) effectiveness of a surgical intervention. This statement was used as a rationale for selecting a five-year time horizon in the model reported by Ackroyd and colleagues.[138] However, the long-term consequences of weight loss may extend beyond the five-year time interval, and result in reduced rates of lifetime mortality and morbidity.[153] Therefore, the lifetime horizon in the models reported in Craig and Tseng,[140] Jensen and Flum[141] and Salem and colleagues[142] is more appropriate for assessing the long-term benefits of bariatric surgery. However, as explained below, these models differ with respect to assumptions about the short-term consequences of bariatric surgery.

Baseline cohort

Van Mastrigt and colleagues[139] reported the baseline characteristics (gender, age, BMI and comorbidities) of the population enrolled in the clinical trial that provided evidence for the economic evaluation of open vertical banded gastroplasty as compared with laparoscopic adjustable gastric banding. Although the population is reasonably well matched across the arms with respect to most of the clinical parameters, there are differences (possibly statistically significant) in relation to the proportion of people in paid employment and (conversely) on disability benefits. In particular, the number

TABLE 42 Model structure/assumptions for cost-effectiveness of alternative treatments of obesity

Author	Ackroyd and colleagues[138]	van Mastrigt and colleagues[139]	Craig and Tseng[140]	Jensen and Flum[141]	Salem and colleagues[142]
New model	Yes	Not applicable	Yes	Yes	Adapted from Craig and Tseng
Type of the economic evaluation	Deterministic decision analytic model	Economic evaluation alongside a clinical trial	Deterministic decision analytic model (a decision tree)	Deterministic decision analytic model (a decision tree)	Deterministic decision analytic model (a decision tree)
Time horizon/ duration of the study	Five years	One year	Lifetime (unspecified)	Lifetime (unspecified)	Lifetime (unspecified)
Baseline cohort	At the baseline in both arms of the model 100% of patients have Type 2 diabetes and BMI > 35	Not applicable	Cost-effectiveness analysis seems to have been conducted separately for cohorts of men and women in the different age categories (between 35 and 55 years with 10-year increments) and different baseline BMI values (between 40 and 50 with an increment of 5 units)	Open GBP group: white women; baseline age 18 years; surgery at the age of 40 and BMI of ≥40. Diet and exercise group: white women; age 18 years; baseline BMI of 33 (or 35)[b]	A set of ICER estimates comparing LGBP with no-treatment and LAGB with no-treatment have been conducted separately for cohorts of men and women: aged 35 with BMI = 40; aged 45 with BMI = 50; aged 55 with BMI = 60
Assumption, main clinical outcomes and how the intermediate outcomes are translated into the final outcomes	Outcomes of bariatric surgery are assessed in terms of weight loss and Type 2 diabetes remission. The probability of developing other obesity-related comorbidities and corresponding changes in life expectancy are implicitly assumed to be the same as in the non-surgical treatment arm. Operative, all cause and comorbidity-related mortality rates are implicitly assumed to be zero. In each year in each arm of the model the Type 2 diabetes outcome is independently assessed as a change from the baseline in proportion of patients free of Type 2 diabetes. This is called an 'annual marginal Type 2 diabetes-free-year gained at a particular year'.	In this non-modelled economic evaluation the EQ-5D[c] utility values were collected from each surviving patient at the baseline, and at 3, 6 and 12 months. To obtain a QALY for each patient the EQ-5D scores were multiplied by the duration of time to which these scores were related. The mean QALY values for each of the treatment alternatives are used in the ICER. The direct and indirect medical cost data were collected from the observational study undertaken to estimate the cost of surgeries, the hospital's billing system, and patients' diaries.	In the no-treatment arm of the model it was assumed that patients do not lose or gain weight, i.e. they remain at the baseline BMI. Life expectancy depends on: (1) BMI value (reduced as result of a successful surgery and stabilised at five years after surgery, or reversed to the baseline value as a result of a reversal surgery); (2) gender; and (3) the age at which the surgery was undertaken. Life expectancy was adjusted for the estimated operative mortality. Utility values (also differentiated by BMI, gender, and age) are applied to the estimated LYs spent with the eventual BMI to obtain QALYs.	Life expectancy depends on BMI, which increases with age, following a trajectory of the obese population (at the rate observed in general USA population in the 95th percentile for weight). In the base case this rate is applied to all surviving patients in each branch of the decision tree. However, the BMI reduction obtained as a result of the GBP (at the age of 40) or a diet and exercise programme (as a result of a one-year programme undertaken at the age of 18) is retained for life. As a result the BMI in such patients, although increasing at the above rate, is always reduced by the incremental BMI value observed after the intervention.	In the no-treatment arm of the model it was assumed that patients do not lose or gain weight, i.e. they remain at the baseline BMI. Life expectancy depends on: (1) BMI value (reduced as result of a successful surgery and stabilised at three years after surgery, or reversed to the baseline value as a result of a reversal surgery); (2) gender; and (3) the age at which the surgery was undertaken. Life expectancy was adjusted for the estimated operative mortality. Utility values (also differentiated by BMI, gender and age) are applied to the estimated LYs spent with the eventual BMI to obtain QALYs.

TABLE 42 *Model structure/assumptions for cost-effectiveness of alternative treatments of obesity (continued)*

Author	Ackroyd and colleagues[138]	van Mastrigt and colleagues[139]	Craig and Tseng[140]	Jensen and Flum[141]	Salem and colleagues[142]
	The cumulative Type 2 diabetes-free years are calculated by aggregating the proportion of patients free from Type 2 diabetes in each year over 5 years.[a] Utility weights are derived from the linear combination of BMI values and the Type 2 diabetes status. QALYs are obtained by aggregating the estimated utility values (according to the BMI and % of Type 2 diabetes-free patients observed in each year) over five years.	The productivity loss was estimated using the friction cost method (not elaborated). The total cost for each patient was calculated as direct and indirect medical cost and the mean total costs for each of the treatment alternatives are used in the ICER.	The arbitrary assigned utility values are applied to the period of time spent in the hospital and in recovering. It was also assumed that the patients who underwent the reversal surgery have 'never [psychologically] recovered completely'. A 50% reduction in utility weights was applied to these patients for the rest of their lives.	Utility values (as a function of BMI) are taken from the published literature.[152] Utility values are assigned according to the BMI observed in each year to obtain QALYs.	The values are taken directly from the study by Craig and Tseng, 2002.[140]
Structure of the model	Not reported. It appears that the cost and effectiveness parameters are assigned to each year independently and then aggregated over five years producing either years free from Type 2 diabetes or QALYs. The cost data were collected from the published literature and expert opinion and assigned to the first year (intervention).	Not applicable	The open GBP arm of the decision tree model assumes four surgery outcomes that occur in the first instance: successful surgery, revision surgery, reversal surgery and death. Revision surgery and reversal surgery are in turn associated with probability of a postsurgical death, while the former may be followed by a subsequent reversal surgery, which is also associated with the probability of death. It is implicitly assumed that the initial and subsequent interventions take place within five years after which the reduced postsurgical BMI is either stabilised or reversed to the baseline value in the unsuccessful surviving patients.	The open GBP arm of the decision tree model assumes two outcomes that occur in the first instance: surgery with immediate complications (undefined), and surgery without immediate complications. Both outcomes are associated with probability of death. The surviving patients may have a reduced BMI or remain with their initial BMI. The diet and exercise arm of the decision tree model assumes that no patient experiences complications associated with death. The surviving patients from the control arm follow the pathway corresponding to the no-complication branch in the open GBP arm of the decision tree.	Both surgery intervention arms of the model assume two outcomes that occur in the first instance: successful surgery, and death. In the LGBP arm the surviving patients may need to undergo a revision surgery, which can be successful or can result in the death of a patient. In the LAGB arm the surviving patients may need to undergo a reversal surgery (band removal), which is not associated with the risk of death. All surviving patients in both arms (except those who underwent a reversal surgery) achieve weight loss specific to the type of surgery.

Author	Ackroyd and colleagues[138]	van Mastrigt and colleagues[139]	Craig and Tseng[140]	Jensen and Flum[141]	Salem and colleagues[142]
Parameters used in sensitivity/scenario analysis (if any)	Simultaneously BMI reduction; % patients free of Type 2 diabetes; (by implication the utility weights have also changed).	Only cost estimates were subjected to the set of one-way sensitivity analyses. These were: operation room personnel cost per minute and unit price of an inpatient day.	% of excess weight lost; reimbursement rate; lifetime medical cost; life expectancy (it was assumed that life expectancy is not affected by the weight loss – i.e. the estimate that corresponds to the baseline weight were apparently used); regression coefficients in the (unreported) multiple regression equation for the utility values were decreased by 25%; operative mortality; complication rates. In the two-way sensitivity analysis the discount rate was increased from 3% to 5% while the lifetime medical cost was assumed to be zero. Another two-way sensitivity analysis varied the estimate of weight loss and the medical cost adjusted for the different reimbursement rates.	A series of one-way sensitivity analyses were performed (the list of parameters tested was not provided). The results proved to be sensitive to the estimated cost of complications (the range tested in the sensitivity analysis was not reported) and the discount rate (neither the value nor the range were reported).	% of excess weight lost; cost of the surgical procedure; number of times a band adjustment was required in the LAGB arm; rates of abdominoplasty; rates of cholecystectomy; operative mortality; rates of revision surgery; rates of reversal surgery in the LAGB arm; a two-way sensitivity analysis was conducted where clinical effect (%EWL) was varied simultaneously in both arms of the models comparing LAGB with no treatment and LGBP with no treatment.
Scenario analysis	The simultaneous reduction in both effectiveness estimates by 20% is called a 'worst case scenario', which is in fact a two-way sensitivity analysis. Both the weight loss (in BMI) and decreased Type 2 diabetes prevalence were reduced by 20% (which is equivalent to assigning a zero benefit in terms of Type 2 diabetes to a non-surgical treatment arm). Cost estimates seem to have been excluded from the scenario/ sensitivity analysis.	The base-case analysis was conducted from the societal perspective. An alternative perspective (presumably that of the Netherlands health-care system) was undertaken when non-medical costs (paid and unpaid help + productivity change) were excluded and the sensitivity of the outcomes to the change of the perspective in the economic evaluation was tested.	The total cost incurred by the payer(s) (the third party + patient's contributions?) was reduced by the median reimbursement rate, which is effectively an equivalent to the change of the perspective of economic evaluation from the unspecified payer's to that of the individually insured patient (who contributes copayments to the total cost).	Best case scenario: patients remained at the exact BMI that they had achieved at the end of the follow-up. Worst case scenario: all weight lost was regained within three years, and the weight gain trajectory of the upper 4.4% was then followed.	None reported

BMI, body mass index; EQ-5D, European Quality of Life-5 Dimensions; EWL, excess weight loss; GBP, gastric bypass; ICER, incremental cost-effectiveness ratio; LAGB, laparoscopic adjustable gastric bypass; LGBP, laparoscopic gastric bypass; LYs, life years; QALY(s), quality-adjusted life-year(s).

a The same algorithm was applied to the second 'annual marginal effectiveness' outcome expressed in kg/m² × year. Unlike years free of Type 2 diabetes, clinical or economic meaning of the outcome expressed in kg/m² × year is not clear therefore it is excluded from further consideration.

b There is a discrepancy in the reported baseline BMI.

c EQ-5D, a generic preference-based health-status measure

of patients claiming disability benefits at baseline was four times higher in the open vertical banded gastroplasty than in the laparoscopic adjustable gastric banding arm. There appears to be a statistically significant difference in the baseline utility values in favour of the laparoscopic adjustable gastric banding arm that may reflect the difference in the level of disability observed at the baseline.

The clinical effectiveness data in the two arms of the model presented in Jensen and Flum[141] were collected from populations of different ages and from different countries.[89,150] It is not clear whether the data for the open gastric bypass arm of the model came from the subgroup of the open GBP patients or from patients who underwent any type of bariatric surgery.[89] The authors acknowledged that the strong assumption of the model is that 18-year-old women with BMI > 33 (or 35) (see *Table 41*, footnote d) are the same individuals who continue gaining weight until they reach BMI > 40 at the age of 40, at which point they undergo open GBP.

In the study by Craig and Tseng[140] the baseline cohort is described as non-smoking adults without a CVD, drug addiction or major psychological disorder and who failed conservative therapies consisting of dieting, exercise, behaviour therapy and pharmacotherapy. The age of the patients is said to be between 35 and 55 years and BMI > 40 and < 50. However, the clinical evidence for the open gastric bypass arm was obtained from a single case series study involving 608 obese patients with BMI ≥40 or BMI ≥35 with comorbidities such as diabetes, arthritis or cardiopulmonary failure.[148] The age of the patients in this study ranged from 14 to 64 (mean age at the time of surgery was 37.3 years). This inconsistency between the definition of the target population for whom bariatric surgery is typically recommended and characteristics of the population used as a source of clinical evidence is likely to undermine the internal validity of the results of the study.

Both Craig and Tseng[140] and Salem and colleagues[142] assumed that patients in the non-surgical treatment arm retain the baseline weight for life. The same assumption, beginning from the second year, was also made in the model reported in Ackroyd and colleagues.[138] This may not be a realistic assumption because patients in the non-treatment arm are likely to continue gaining weight during their lifetime, as assumed in the model reported by Jensen and Flum.[141] The assumption of zero weight gain over the modelled time interval in patients in the non-surgical treatment arm is likely to bias the cost-effectiveness estimates although the direction of the potential bias is uncertain.

Assumptions about the short-term and long-term consequences of surgical interventions

The immediate consequences of surgical interventions are associated with the risk of operative death and complications that may occur during the postsurgery recovery such as deep venous thrombosis and wound infection, which do not typically require a surgical intervention. Other complications such as staple-line disruption or dehiscence may require a revision or even a reversal surgery. Reversal surgery is also required when patients cannot restrict their diets sufficiently following surgery and develop intractable dumping syndrome. In addition, nearly a quarter of patients require treatment for incisional hernia within two years after hospital discharge. Some patients require treatment for cholelithiasis two years after discharge and abdominoplasty five years after discharge.[140]

Ackroyd and colleagues[138] do not model the differential rates of postsurgical complications for laparoscopic adjustable gastric banding, open gastric bypass and non-surgical treatment (where they are, by definition, zero). However, the differential use of resources is included in the cost side of the cost-effectiveness estimate. The decision analytic models reported by Jensen and Flum,[141] Salem and colleagues,[142] and Craig and Tseng[140] all include differential probabilities associated with operative mortality and complications, especially those that require surgical interventions and are associated with the risk of death. Jensen and Flum[141] only include immediate (unspecified) complications while Salem and colleagues[142] and Craig and Tseng[142] model postoperative complications over three-year and five-year time intervals, respectively. In these studies the operative mortality is factored into calculations of LY estimates.

The postoperative complications in surviving patients are likely to result in a temporary reduction in QoL. The study by Craig and Tseng was the only one that attributed disutility values to patients who experienced postoperative complications, but only to those complications that required a surgical intervention (see section on Translation of short-term outcomes into final outcomes, this chapter). Other modelled economic

evaluations do not fully incorporate the differential rate of postoperative complications in surviving patients.

The long-term outcomes of bariatric surgery include the reduced probability of developing an obesity-related disease. In particular, remission of Type 2 diabetes is frequently observed in obese patients who successfully underwent bariatric surgery. In Ackroyd and colleagues,[138] which includes only patients with Type 2 diabetes at baseline, the clinical effectiveness data for each of the five years appear to have been extracted from the various studies with different cut-off points and different characteristics of the obese population. It appears that the implicit assumption of the model is that for each patient the probability of Type 2 diabetes remission in each year does not depend on the Type 2 diabetes status in the previous year or on the BMI. This assumption may not be reasonable.

Jensen and Flum,[141] Salem and colleagues[142] and Craig and Tseng[140] do not explicitly model the differential probabilities of developing an obesity-related disease. However, the gender- and age-specific life expectancy estimates used in these studies are taken from the published model by Thompson and colleagues[144] that includes the lifetime risks of hypertension, hypercholesterolemia, Type 2 diabetes, coronary heart disease (CHD) and stroke in relation to BMI.

Translation of short-term outcomes into final outcomes

Typically, to obtain final outcomes such as QALYs the duration of time that a patient spends in a particular health state is 'weighted' using a utility estimate (typically ranging from 0 = death to 1 = perfect health) that corresponds to this health state. This approach was used in assessing the cost-effectiveness of pharmacotherapies for obesity treatment as compared to non-pharmaceutical treatment options.[154]

The modelled economic evaluations of bariatric surgery do not explicitly define health states in terms of disease progression but either derive the utility estimates from the regression analysis that estimated the relationship between utility [measured in European Quality Of Life-5 Dimensions (EQ-5D) values] and BMI values while accounting for the Type 2 diabetes status,[138] or used the published utility estimates for the general population,[155] and for the overweight population.[152]

The utility weights are then applied to the cohort of surviving obese patients as they progress through the modelled time interval.

The second component (life expectancy) that is required to calculate QALYs in the modelled economic evaluations with a lifetime horizon[140–142] was obtained from a single published source,[144] which reports life expectancy for the US population categorised by age and BMI.

Estimation of utility values
There are variations between the studies in the methods adopted for estimating utility values.

In van Mastrigt and colleagues[139] the EQ-5D utility values were collected from each surviving patient at the baseline, and at three, six and 12 months. To obtain a QALY for each patient the EQ-5D scores were multiplied by the duration of time (as a proportion of the 12-month time interval) to which these scores related. The mean QALY values for each of the treatment alternatives were used in the denominator of the ICER.

Ackroyd and colleagues[138] utility values were estimated using the empirical data on the representative sample of the UK population ($n = 13,500$), that included both obese and non-obese individuals.[156] The data were used to estimate a linear relationship between the EQ-5D values and BMI values. The authors do not justify the linearity assumption in their estimate of the relationship between the observed utility and BMI values. As is evident from Figure 1 in Ackroyd and colleagues,[138] while this assumption may be true in the general UK population, in relation to the obese population with BMI > 35, a more complex form of regression equation may be more appropriate.

It appears that at first the coefficients in the linear regression of utility values on BMI values were estimated separately for Type 2 diabetes and non-Type 2 diabetes subgroups. The authors then assumed that there was no statistically significant difference in the estimated regression coefficients (slopes) in these two equations. Therefore the alternative (not reported) regression equations were used to estimate utility values in both subgroups. It seems that the modified regression equations have different constant terms (from the original equations), but the same slope equal to the weighted average of the slopes in regression equations for two separate subgroups. This is not a correct way of deriving utility estimates that may vary with respect to both BMI and Type 2

diabetes. A multiple regression of utility values on BMI values and Type 2 diabetes status and an interaction term (BMI × Type 2 diabetes) would be more appropriate.

The QALY outcomes in the study by Ackroyd and colleagues[138] were obtained by combining the utility estimates for the mean BMI reduction observed in any particular year in Type 2 diabetes and non-Type 2 diabetes patients and then aggregating the calculated values over the five-year time interval.

Craig and Tseng[140] do not report clearly the method used for obtaining utility values for the specified cohorts of men and women in the different age categories and baseline BMI values. From their reference it can be deduced that utility values might have been elicited using the published algorithm which employed data from the 1997 USA National Health Interview Survey.[155] The population-based mean values describing the Activity Limitations and Perceived Health Status were then interpreted as single attribute scores of a two-dimensional generic QoL instrument. A modelling technique was used to obtain the missing multiple attribute scores (e.g. for the combination of Activity Limitations and Perceived Health Status values). The resulting utility values are assumed to reflect HRQoL in the US general population. These values were not available for the population categorised by age, gender and BMI, which limited the possibility of using the estimates of life expectancy for the general population categorised by gender, age and BMI values.[144]

It is not clear whether Craig and Tseng[140] fully replicated the complex modelled calculations reported in Erickson and colleagues[155] with respect to the population data stratified by age, gender and BMI. It is possible that some methodological shortcomings were overlooked in the process. For example, Erickson and colleagues estimated that in the US general population of 35–40 years old the utility value is 0.89. According to Craig and Tseng,[140] the overweight 35-year-old men and women (i.e. with BMI of 25) have utility values of 0.93 and 0.91 respectively. It then follows that the overweight population in this age group has a higher HRQoL than the general US population. This contradicts the authors' statement that their findings indicate that there is a negative relation between HRQoL and BMI.

Nevertheless, the newly estimated utility values were then applied to the estimated age/gender/

BMI-specific life expectancy[144] to obtain QALYs. The shortcoming of this approach is that first, the utility weights were not obtained using one of the conventional techniques for eliciting population-based health preferences (standard gamble or time trade-off) and second, that the utility weights were not elicited from the obese population, whose health-related preferences may be different from those of the general population.

The study by Craig and Tseng[140] was the only one among the identified modelled economic evaluations that attempted to incorporate the differential rates of surgical complications on both the cost and the effectiveness sides of the ICER. It was reasonably assumed that there is a reduction in QoL (disutility) associated with postsurgical complications. In the absence of published evidence, Craig and Tseng[140] assigned some arbitrary utility values to the period of time spent in hospital and in postsurgery recovery. It was implicitly assumed that non-surgical complications are not associated with a reduction in QoL. For the period of a hospital admission the corresponding age/gender/BMI-specific utility value was reduced by 200% (assuming that being in hospital is equivalent to a health state which is significantly 'worse than death'). The utility value associated with the recovery time was 50% of the applicable utility value. The utility weights which apply to the remaining years of life in patients who underwent a reversal surgery were also reduced by 50% (it is assumed that patients never recovered completely from reversal surgery because of its psychological effects). No justification for the choice of these values was provided.

Salem and colleagues[142] replicated the method of converting the intermediate clinical outcomes (weight reduction) into QALYs introduced by Craig and Tseng[140] and used the utility values from their study. Therefore the methodological shortcomings that characterise the study by Craig and Tseng[140] also apply to the study by Salem and colleagues.[142]

In both studies by Craig and Tseng[140] and by Salem and colleagues[142] the gender-specific utility weights change over time as the age of the cohort increases. However, utility weights do not change with respect to the BMI value that remained fixed at the baseline level in the non-surgical treatment arm, and in the surgery arm, at the level achieved when the postsurgical interventions (e.g. band adjustments, revision and reversal surgeries) are completed.

In contrast, the study by Jensen and Flum[141] does not make an assumption about the BMI values remaining unchanged during the patients' lifetime. The trajectory of weight increase was estimated from the data on the BMI distribution in the US white female population stratified by age.[157] In the base-case scenario BMI values increase from one year to another at the rate observed in the general USA population in the 95.6th percentile for weight (a cut-off point for BMI > 40, which corresponds to 4.4% of the population at age 40). In the base case this rate is applied to all surviving patients in each branch of the decision tree. However, the BMI reduction obtained as a result of the open GBP or a diet and exercise programme is retained for life. As a result, the BMI in such patients, although increasing at the above rate, is always reduced by the incremental BMI value observed after the intervention. Utility values used in this study were obtained from the study by Hakim and colleagues,[152] who estimated a utility gain associated with each unit of BMI lost. The utility values were then combined with life expectancy data.[144] QALYs gained in each arm of the model are totalled each year. The authors commented that this yearly calculation, rather than assigning a single estimate of the life expectancy based on the BMI observed at the end of the intervention period, is necessary because the interventions take place at different times and BMI is assumed to be increasing over time.[141]

Life expectancy and lifetime medical cost estimates

As was mentioned before, all modelled economic evaluations with the lifetime horizon[140–142] applied utility values to the life expectancy estimates for the US population categorised by age, gender and BMI.[144] Thompson and colleagues[144] reported both the life expectancy estimates and the lifetime medical cost estimates that were also used in all modelled economic evaluations. The estimates are based on the USA Third National Health and Nutrition Examination Survey (1988–94) that was provided separately for men and women categorised by age groups from 35 to 64 years in 10-year increments. However, Thompson and colleagues[144] report the life expectancy estimates only up to BMI of 37.5, which is below the range of BMI values assessed in the modelled economic evaluations.

Craig and Tseng[140] and Salem and colleagues[142] applied what they described as 'a simple linear approximation' to obtain life expectancy for the BMI values beyond the range reported in

Thompson and colleagues.[144] Although no further details were provided, it appears that the method was insufficient to obtain reliable estimates of life expectancy. For example, Thompson and colleagues[144] reported life expectancy of men aged 59.5 years (midpoint in the age group of 55–64 years) with BMI of 37.5 to be 18.3 years. It is reasonable to assume that the life expectancy of men aged 55 with BMI of 37.5 is likely to be higher than this.

According to the calculations by Craig and Tseng,[140] life expectancy of 55 year old men with BMI of 40 from the 'no treatment' arm is 16.15 years. This implies that the additional weight of 2.5 BMI is associated with the loss of at least 2.15 years of life. According to Thompson and colleagues[144] for men in the 55–64-year age group the additional weight gain of five BMI units (from 32.5 to 37.5 kg/m²) is associated with the loss of just 0.5 years of life (from 18.8 to 18.3 years). Although it is possible that the lesser increments in weight gain when applied to the higher BMI values are associated with the accelerated loss of years of life, the difference in the estimates of additional LYs lost as the result of obesity is too large to be plausible and is more likely to relate to a deficiency in the methods used by Craig and Tseng[140] to extrapolate life expectancy values to the higher BMI categories. It is therefore likely that the study by Craig and Tseng[140] has produced biased estimates of the final outcomes.

Salem and colleagues[142] do not report the estimated life expectancy values obtained by method of 'a simple linear approximation', so it is not possible to assess their validity.

Jensen and Flum[141] also used a 'linear approximation' to obtain life expectancy for each BMI value not reported in Thompson and colleagues.[144] The linear regression equation that relates the remaining years of life to the BMI value is provided. It appears that only a subset of the data reported in Thompson and colleagues[144] (i.e. the life expectancy data for women in the 45–54-year-old category) was used in the regression. How accurate the linear fit is in relation to other subgroups of the female population is not clear.

The final outcomes (LYs and QALYs) reported in the identified economic evaluations are presented in *Tables 45* to *47* in the section on Results reported in the identified economic evaluations of bariatric surgeries in this chapter.

Structure of the models

The structure of the decision tree models reported in the studies by Craig and Tseng,[140] Jensen and Flum[141] and Salem and colleagues[142] are presented in a graphical format. The study by Ackroyd and colleagues[138] does not explicitly present the structure of their deterministic model.

Craig and Tseng[140] have assumed that in the first instance four alternative outcomes of open gastric bypass can occur simultaneously: a successful surgery, a revision surgery, a reversal surgery and death. Revision surgery and reversal surgery are in turn associated with the probability of a postsurgical death, while the former may be followed by a subsequent reversal surgery, which is also associated with the probability of death. Although it may be reasonable to assume that in some patients revision surgery may be undertaken immediately to correct the complications arising in the course of the initial surgery, other surgical interventions (e.g. abdominoplasty) may occur over a period of three to five years. It is not clear how these later surgeries are incorporated into the model. Also, the decision to undertake a reversal surgery may be separated in time from the initial surgery. The modelling assumptions in Craig and Tseng[140] may not correspond to current clinical practice.

The structure of the model presented in Salem and colleagues[142] seemed to be an improvement in comparison to the structure of the model presented in Craig and Tseng.[140] Salem and colleagues[142] have assumed that the immediate outcome of bariatric surgery is either survival or death, therefore the probabilities of revision or reversal surgeries apply only to the surviving patients.

The decision tree model reported in Jensen and Flum[141] has the following options: 'Intervention with immediate complications'; 'Intervention without immediate complications'; 'Death'; 'Alive with reduced BMI'; and 'Alive with baseline BMI'. The probability values associated with each outcome are not reported. No details on the types of immediate complications are provided. It is reasonably assumed in the diet and exercise arm of the decision tree that no patient experiences complications associated with death. The surviving patients in both arms of the model may have a reduced BMI or remain with their initial BMI.

The shortcoming of the model is the exclusion of non-immediate complications, which among other things, rules out the probability of revision surgeries that occur later in time and are also

associated with the risk of death. Therefore the modelling assumptions in Jensen and Flum[141] may not correspond to current clinical practice.

Estimation of costs within economic evaluations

Cost of bariatric surgeries

A comprehensive itemised list of health-care resources used and the corresponding unit costs were not provided in the identified studies on economic evaluation of bariatric surgery. The most detailed account of health-care resources used in laparoscopic gastric bypass and laparoscopic adjustable gastric banding is reported in Ackroyd and colleagues.[138] It seems that for each type of surgical intervention the range of resource items was identified, checked with experts and multiplied by the corresponding unit costs. However, the list of resource components in natural units does not include the itemised cost of complications. It is not clear how the cost of postsurgical complications was estimated.

Ackroyd and colleagues[138] employed different methods for producing the cost estimates in relation to three European countries, which makes the comparison of cost data across these countries problematic. Therefore, only the UK cost data as reported in Ackroyd and colleagues[138] are included in this section.

Van Mastrigt and colleagues[139] estimated resources used in laparoscopic adjustable gastric banding and open vertical banded gastroplasty in natural units by conducting an observational study of 10 surgical procedures of both types of surgery. Other hospital costs were obtained from the hospital's billing system. Health-resource items used outside the hospital (e.g. medications used during the follow-up) were obtained from the patients' cost-diaries. The cost of each of the postsurgical complications was not reported. However, the aggregated mean cost of rehospitalisations is provided and is likely to relate to the number and seriousness of postsurgical complications associated with each surgery.

Table 43 summarises the cost data in terms of the natural units and the corresponding unit costs because this is a conventional approach to reporting cost data. Cost data by unit costs for the selected cost items are reported in Ackroyd and colleagues[138] and in van Mastrigt and colleagues[139] along with other cost data that are reported in more aggregated cost categories. These are also included for completeness.

Craig and Tseng[140] and Salem and colleagues[142] reported aggregated cost categories for bariatric surgery, postsurgical complications, revision and reversal surgery using the US Healthcare Cost and Utilisation project database (1997).[158] The costs were then adjusted for inflation using a medical-care component of the consumer price index. No further details were reported.

Jensen and Flum[141] used the published cost data from a single study comparing open gastric bypass with laparoscopic gastric bypass.[113] The missing estimate of the cost(s) of complications was set to be $5000 per complication, which appears to be an underestimate. The costs were then adjusted for inflation to 2004 US prices using the Bureau of Labour Statistics Inflation calculator. It is not clear whether this method is an equivalent to the correct method of using a medical-care component of the consumer price index as in the other US studies.[140,142] Costs for the comparator treatment – a one-year programme of diet and exercise – were taken from the US case–control longitudinal study by Heshka and colleagues.[150] Health-care resources and the corresponding unit costs are reported only for the comparator arm of the model and no direct medical costs of bariatric surgery are reported, therefore this study is excluded from the cost data analysis presented below.

It should be noted that although in different studies the same name may be used to identify an aggregated cost component, the health-care resources included under this category may be quite different. Therefore, no meaningful comparison across the studies with respect to the individual cost items can be made. Comparisons with respect to the total costs are also limited because of differences in the nature of the health-care systems (i.e. private versus public) and because of differences in the currencies in which costs are reported (see *Table 41*).

According to Ackroyd and colleagues,[138] the direct medical costs of laparoscopic gastric bypass and laparoscopic adjustable gastric banding over five years do not appear to be different. Likewise, van Mastrigt and colleagues[139] found no statistically significant difference in the mean costs of laparoscopic adjustable gastric banding and vertical banded gastroplasty over a one-year time interval.

Only a very limited number of cost components, (i.e. those reported in natural units) are available for direct comparison between the studies. According to Ackroyd and colleagues,[138] the

mean LOS for the initial surgery is not very different between laparoscopic gastric bypass and laparoscopic adjustable gastric banding and is about five days. The study by van Mastrigt and colleagues[139] reported the mean estimate of the LOS for the initial laparoscopic adjustable gastric banding as 5.56 days, which is about 0.5 days longer than the corresponding LOS reported in Ackroyd and colleagues.[138] However, van Mastrigt and colleagues[139] found that the median LOS was only four days, which is one day shorter than the mean LOS reported in Ackroyd and colleagues.[138] The discrepancy between the mean and median LOS reported in van Mastrigt and colleagues[139] is likely to have resulted from the relatively small sample of the population participating in the study (50 patients in each arm). The sample size used in the LOS estimate in Ackroyd and colleagues[138] was not reported. It is therefore uncertain which of the estimates is more accurate. The same concern also applies to the duration of the operating theatre time to conduct laparoscopic adjustable gastric banding surgery, which is reported as 1.9 hours and 3.26 hours, respectively, in the studies by Ackroyd and colleagues[138] and van Mastrigt and colleagues.[139]

Table 44 summarises the cost data as reported in two US studies by Craig and Tseng[140] and by Salem and colleagues.[142] In comparison to Ackroyd and colleagues[138] and van Mastrigt and colleagues,[139] the US studies[140,142] provide a more elaborate list of postsurgical complications and associated direct medical costs. Direct comparison of the cost estimates across these studies is not possible because they do not involve a common surgical intervention and employ different formats for reporting cost estimates: Craig and Tseng[140] report the costs by gender categories while Salem and colleagues[142] do not differentiate the costs by gender. Both studies[140,142] report health-care resources used in bariatric surgery by aggregated cost categories, the only resource reported in natural units is the number of follow-up visits, which is three times a year for three years for open gastric bypass according to Craig and Tseng[140] and twice a year for three years for laparoscopic gastric bypass according to Salem and colleagues.[142] The latter study also reported that the expected number of band adjustments over three years following laparoscopic adjustable gastric banding is 10. Both studies report only point estimates without a 95% CI, which limits the possibility of establishing the statistical significance of the difference in costs of bariatric surgeries.

TABLE 43 Use of health-care resources in bariatric surgery (natural units and the corresponding unit costs) as reported in Ackroyd and colleagues[138] and van Mastrigt and colleagues[139]

Cost components	Type of health-care resources by the type of surgery	Mean number of units (source)	Unit cost (source)	Aggregated costs: laparoscopic gastric bypass (source)	Aggregated costs: laparoscopic adjustable gastric banding (source)	Aggregated costs: vertical banded gastroplasty (source)
Preoperative evaluation	n/a	n/a	n/a	£610[138]	£610[138]	n/a
Diagnostic procedures	n/a	n/a	n/a	£187[138]	£492[138]	n/a
Hospital stay for the initial surgery	Bed use (LGBP)	LOS = 4.88[138]	Cost per day = £235[138]	235 × 4.88 = £1147[138]		
	Bed use (LAGB)	LOS = 5[138]	Cost per day = £241[138]		241 × 5 = £1205[138]	
	Bed use (LAGB)	LOS = 5.56[a,139]	Cost per day = €332[139] (LAGB and VBG)		332 × 5.56 = €1846	
	Bed use (VBG)	LOS = 6.78[a,139]				€2251[139]
Operating room costs	Hours (LGBP)	3.84[138]	Operating theatre personnel cost per minute was not reported	n/a	n/a	n/a
	Hours (LAGB)	1.9[138]				
	Hours (LAGB)	3.26[139]	Operating theatre personnel cost per minute = €2.96[139] (LAGB and VBG)	€579	n/a	
	Hours (VBG)	2.50[139]				€444
Operating room overheads	n/a	n/a	n/a	£187[138]	£492[138], €87[139]	€87[139]
Surgery specific equipment	Implants (LGBP)	1[138]	£2591[138]	Total cost of surgery-specific equipment and materials is not reported by Ackroyd and colleagues[138]	Total cost of surgery-specific equipment and materials is not reported by Ackroyd and colleagues[138]	n/a
	Implants (LAGB)	1[138]	£1175[138]			

Cost components	Type of health-care resources by the type of surgery	Mean number of units (source)	Unit cost (source)	Aggregated costs: laparoscopic gastric bypass (source)	Aggregated costs: laparoscopic adjustable gastric banding (source)	Aggregated costs: vertical banded gastroplasty (source)
Surgery specific materials (unspecified)[b]	n/a	n/a	n/a	n/a	€2143[139]	€691[139]
Subtotal: cost of initial surgery	n/a	n/a	n/a	n/a	€3861[139]	€1676[139]
Subtotal: cost of initial hospitalisation[c]				£4456[138]	£3315[138], €5954[139]	€5258[139]
Cost of unspecified complications	n/a	n/a	n/a	£45[138]	£296[138]	
Cost of rehospitalisations	n/a	n/a	n/a	n/a	€724[139]	€599[139]
Cost of follow-up	n/a	n/a	n/a	£312[138]	£439[138], €1479[139]	€1426[139]
Total health-care (medical) cost of bariatric surgery[d,e]	n/a	n/a	n/a	£6346[138]	£6060[138], €7336[139]	€8105[139]

LGBP, laparoscopic gastric bypass; LAGB, laparoscopic adjustable gastric banding; LOS, length of [hospital] stay; n/a, not available; VBG, vertical banded gastroplasty.
a van Mastrigt and colleagues, reported the median LOS in both LAGB and open VBG as equal to four days.
b It is not clear whether the total cost of materials also includes the cost of implants.
c It is not clear for van Mastrigt and colleagues whether the total cost of initial hospitalisation includes the preadmission visits and diagnostic procedures.
d For Ackroyd and colleagues the total discounted cost includes the cost of preoperative assessment, cost of initial hospitalisation, total annual follow-up cost for five years and the cost of complications that are likely to occur over the five postsurgery years.
e For van Mastrigt and colleagues the total medical cost is calculated by deducting non-medical costs from the total cost of bariatric surgery estimated from the societal perspective.

TABLE 44 *Health-care resources used in bariatric surgery as reported by Craig and Tseng[140] and Salem and colleagues[142]*

Resource category	Type of resources by aggregated cost categories	Cost estimate of resources used in open GBP (Craig and Tseng[140]) (US$2001)		Cost estimate of resources used in LGBP (Salem and colleagues[142]) (US$2004)	Cost estimate of resources used in LAGB (Salem and colleagues[142]) (US$2004)
		Men	**Women**	**Obese population**	**Obese population**
Cost of surgery		$26,100	$20,500	$27,560	$16,200
	Band adjustment			n/a	$150 per visit × 10 visits over 3 years
Cost of immediate complications requiring surgery	Revision surgery	$38,500	$25,600	$10,000	$5000
	Reversal surgery (band removal)	n/a	n/a	n/a	$6000
	Reversal surgery GBP	$38,500	$25,600	N/R	n/a
Cost of subsequent complications	Minor wound infection	$192	$192	$204	$204
	Major wound infection	$20,600	$19,200	$11,236	$11,236
	Deep venous thrombosis	$8700	$8100	$9222	$9222
	Pulmonary embolism	$14,700	$13,900	$15,582	$15,582
	Leak non-operative	n/r	n/r	$50,000	n/a
	Cholecystectomy	$27,100	$22,700	$16,000	$16,000
	Incisional hernia	$13,200	$12,500	$14,416	$14,416
	Abdominoplasty	$13,600	$12,200	$13,992	$13,992
	Postoperative death	$27,600	$29,000	n/r	n/r
Follow-up cost		$150 per visit × 3 visits a year	$150 per visit × 3 visits a year	$159 per visit × 2 visits a year	None required except for the scheduled band adjustment visits
Lifetime cost of pharmaceuticals		$68	$68	$72	$0

GBP, gastric bypass (as applicable in the context of open GBP or LGBP); LAGB, laparoscopic adjustable gastric banding; LGBP, laparoscopic gastric bypass; n/a, not applicable; n/r, not reported.

Neither Craig and Tseng[140] nor Salem and colleagues[142] report the estimated cost of bariatric surgery that would apply to the general population. The total cost estimates are available only with respect to the subgroups of the population with the selected combination of gender/age/BMI value and no comorbidities at the baseline. Craig and Tseng[140] reported that sex-specific cost estimates were consistently higher in men than in women except for postoperative death, but did not offer any explanation as to the possible reason for the observed cost differences.

The US cost estimates in *Table 44* are not consistent with the cost data presented in *Table 43* in that the mean total cost of laparoscopic gastric bypass

appears to be higher than the mean total cost of laparoscopic adjustable gastric banding although whether this difference reaches the level of statistical significance is uncertain.

There is a large difference in costs of revision surgeries with open gastric bypass revision in men being four times more expensive than laparoscopic gastric bypass revision and eight times more expensive than laparoscopic adjustable gastric banding revision.[140,142] The cost difference is likely to be the result of the differences between the open and laparoscopic surgeries, and other differences in surgical techniques employed across the bariatric surgeries.

Cost of non-surgical treatment (comparator)

It appears that Craig and Tseng[140] and Salem and colleagues[142] have implicitly assumed that the short-term cost of non-surgical treatment alternatives (such as diet and exercise) is zero. This assumption, although it may not be realistic, is conservative and is likely to bias the ICER in favour of the comparator.

Jensen and Flum[141] provided a detailed account of the health-care resources in natural units and the corresponding unit costs for the comparator treatment – a one-year diet and exercise programme. However, the cost of a single privately run diet and exercise programme undertaken by predominantly white females residing in the USA may be of limited generalisability.

Ackroyd and colleagues[138] provided a fairly comprehensive list of health-care resources used in the comparator arm – a conventional treatment that typically involves dieting (see Table 40, footnote b). The resource use is reported in natural units (e.g. number of GP and dietitian consultations; number of district and practice nurse consultations; number of laboratory assessments and number of food substitutes) and the corresponding unit costs as well as in aggregated cost-categories (an annual cost of outpatient visits, pharmaceuticals and hospital admissions).

The study by Ackroyd and colleagues[138] was the only one among the modelled economic evaluations that explicitly modelled the prevalence of Type 2 diabetes in non-surgical and surgical treatment arms. The cost of treatment of obesity-related Type 2 diabetes was taken from the CODE-2 (The Cost of Diabetes in Europe – Type II) survey which used the 1999 prices,[159] while the cost of surgical interventions is expressed in 2005 prices. It does not appear likely that the cost of a comparator in terms of treatment of Type 2 diabetes was converted into 2005 prices using the health price index. This approach is likely to produce a bias in the cost-effectiveness estimate in favour of surgical treatments.

Long-term costs

The studies by van Mastrigt and colleagues[139] and by Ackroyd and colleagues[138] limited their time horizons to one year and five years, respectively, and did not include any long-term costs and the outcomes of bariatric surgeries.

Three other studies[140–142] used the same published source of the lifetime medical costs for the different subgroups of the US population categorised by age/gender/BMI.[144] These costs were applied to both the surgical and non-surgical treatments. As already mentioned in the section on Translation of short-term outcomes into final outcomes, this chapter, Thompson and colleagues[144] reported the lifetime medical cost estimates separately for men and women categorised by age groups from 35 to 64 years old in 10-year increments. However, the published lifetime medical-cost estimates are available only up to BMI of 37.5 which is below the range of BMI values assessed in the modelled economic evaluations. All authors used a linear extrapolation method to obtain the estimates of the lifetime medical cost for BMI values above the range reported in Thompson and colleagues.[144] Although no actual values of the estimated lifetime medical cost are reported in the studies, the same concerns about the methods used in extrapolating life expectancy estimates, that were outlined earlier may also apply to extrapolating lifetime medical costs.

Results reported in the identified economic evaluations of bariatric surgeries

Tables 45 to 47 present the estimated costs, outcomes and ICERs as reported in the identified studies. Three tables were designed to accommodate the inconsistency in the format of reporting incremental costs and incremental outcomes across the studies. Some studies (most notably Jensen and Flum[141]) do not report costs and outcomes separately for each treatment alternative.

Results reported in Ackroyd and colleagues[138] and van Mastrigt and colleagues[139]

Table 45 presents results reported in Ackroyd and colleagues[138] and van Mastrigt and colleagues[139] with respect to costs and outcomes expressed in QALYs. These two studies adopt different perspectives: Ackroyd and colleagues[138] adopted a payer's perspective (i.e. the NHS in the case of UK) and van Mastrigt and colleagues[139] adopted a societal perspective. The costs in van Mastrigt and colleagues[139] were reduced by us by the amount of non-direct costs to make the results of these two

TABLE 45 *Cost-effectiveness estimates of bariatric surgeries as compared to the alternative treatment strategy as reported in Ackroyd and colleagues[138] and van Mastrigt and colleagues[139]*

Type of treatment strategies	Results				
Intervention and comparator	Cost of the intervention[a]	Cost of the comparator[a]	QALYs intervention[a]	QALYs comparator[a]	ICER (Incremental cost over incremental outcome)
LGBP vs conventional treatment[138]	£9121[b]	£7083[b]	3.34[b]	2.00[b]	2033/1.34 = £1517/ QALY
LAGB vs conventional treatment[138]	£9072[b]	£7088[b]	3.03[b]	2.00[b]	1984/1.03 = £1929/ QALY
VBG vs LAGB (assumed to be a comparator)[139]	€8105[c]	€7336[c]	0.76[d] (SD = 0.2)	0.81[d] (SD = 0.13)	LAGB dominates open VBG

ICER, incremental cost-effectiveness ratio; LAGB, laparoscopic adjustable gastric bypass; LGBP, laparoscopic gastric bypass; LYs, life years; QALY, quality-adjusted life-year; SD, standard deviation; VBG, vertical banded gastroplasty.
a Cumulative discounted cost/outcome over the horizon of the model or the time interval used in the economic evaluation
b See table 13 in Ackroyd and colleagues[138] for the total discounted (at 3.5%) costs accumulated over five years. There is a discrepancy in the costs reported for the first year by Ackroyd and colleagues in table 13 and tables 6 and 7.[138]
c See *Table 43* above and Table 2 in van Mastrigt and colleagues.[139] Discounting rates do not apply.
d The mean difference of 0.05 utility scores between LAGB and open VBG is not statistically significant ($p = 0.138$).

studies comparable (see *Table 43*, footnote e). Both studies undertook cost-effectiveness analyses (CEA) in addition to cost–utility analyses (CUA). These are discussed below.

Ackroyd and colleagues[138] reported that in comparison to non-surgical treatment laparoscopic gastric bypass is associated with an incremental cost of £1517 per QALY, and laparoscopic adjustable gastric banding is associated with an incremental cost of £1929 per QALY. Both costs and outcomes are discounted at 3.5%. With respect to diabetes mellitus outcome, laparoscopic gastric bypass is associated with an additional 2.6 years free of Type 2 diabetes or incremental cost of £776 per Type 2 diabetes-free year, and laparoscopic adjustable gastric banding is associated with an additional 2.5 years free of Type 2 diabetes or incremental cost of £810 per Type 2 diabetes-free year. The outcomes in terms of the Type 2 diabetes prevalence observed over five years were not discounted. It is not clear whether discounted or undiscounted costs were used in calculating ICERs with respect to the Type 2 diabetes prevalence. Ackroyd and colleagues[138] suggested that at five-year follow-up both laparoscopic gastric bypass and laparoscopic adjustable gastric banding are cost-effective in comparison to a non-surgical treatments in patients with Type 2 diabetes and a baseline BMI > 35.

Van Mastrigt and colleagues[139] used the observational data collected alongside an RCT involving 100 patients undertaking either laparoscopic adjustable gastric banding or open vertical banded gastroplasty and reported the 12-month outcomes in terms of % excess weight loss (EWL) and QALYs. A bootstrap analysis of the joint distribution of incremental costs and outcomes involving 1000 replications identified that in 86% of trials laparoscopic adjustable gastric banding was both less effective and less expensive in comparison to open vertical banded gastroplasty, and in 14% of trials it was less effective and more expensive (i.e. dominated by open vertical banded gastroplasty). The authors erroneously claimed that moving from open vertical banded gastroplasty to laparoscopic adjustable gastric banding would involve an additional amount of €105.80 per each additional %EWL. In fact, this amount is what society would be spending for choosing not to switch from open vertical banded gastroplasty to laparoscopic adjustable gastric banding, i.e. replacing open vertical banded gastroplasty with laparoscopic adjustable gastric banding would involve a saving of €105.80 for each per cent of extra weight retained.

With respect to the outcomes expressed in QALYs a different (and somewhat contradictory) result was reported: laparoscopic adjustable gastric banding

appears to be both less expensive and more effective than open vertical banded gastroplasty (i.e. a dominant strategy). A bootstrap analysis showed that in 79% of trials laparoscopic adjustable gastric banding was both more effective and less expensive in comparison to open vertical banded gastroplasty (i.e. dominant); and in 14% of trials it was more effective but also more expensive. There was a negligible probability of open vertical banded gastroplasty being dominant (3%) or being both less effective and less expensive (4%).

The authors suggested that the difference in QALYs at 12 months after surgery was not statistically significant between the open vertical banded gastroplasty and laparoscopic adjustable gastric banding arms. Although the observed utility scores at 12 months do appear very similar between the arms these values do not reflect the baseline difference (see discussion in section on Assumptions of economic evaluations, this chapter). The absolute utility values were not reported, but as is evident from Figure 3 in van Mastrigt and colleagues,[139] the incremental utility gain over 12 months appears to be larger in the open vertical banded gastroplasty arm. Without the long-term data it is not possible to say whether the larger incremental gain associated with open vertical banded gastroplasty would extend beyond the first year. However, these considerations undermine the long-term validity of the authors' conclusions of no incremental gain in QALYs between the open vertical banded gastroplasty and laparoscopic adjustable gastric banding and the laparoscopic adjustable gastric banding dominance with respect to open vertical banded gastroplasty.

Inconsistently with the results of their CEA the authors concluded that at 12 months the costs and QALYs outcomes of two alternative surgical interventions were found to be equal.[139] Therefore the selection of the procedure should be based on the clinical aspects, efficacy and safety at one year.

Results reported in the US studies by Jensen and Flum,[141] Craig and Tseng[140] and Salem and colleagues[142]

Table 46 presents results reported in Jensen and Flum.[141] The studies by Craig and Tseng[140] and Salem and colleagues[142] are reported separately in *Table 47*.

On the basis of the results reported in Jensen and Flum,[141] open gastric bypass appears to be cost-effective at the incremental cost of $7126 per QALY, although the incremental effect is reported in terms of additional LYs gained rather than QALYs. The ICER reported by Jensen and Flum[141] comparing open bastric bypass undertaken by white females at the age of 40 (BMI > 40) with a diet and exercise programme undertaken at the age of 18 [BMI > 33(or 35); see *Table 41*, footnote d] falls within the range of ICERs reported by Craig and Tseng for the subgroups of females aged 35 or 55 and with the baseline BMI of 40 or 50 (see *Table 47*).

Table 47 presents results reported in Craig and Tseng[140] and Salem and colleagues.[142] The results are reported with respect to subgroups of population with the specified baseline characteristics of gender/age/BMI.

The results reported by Craig and Tseng[140] are characterised by large variability with respect to baseline demographic characteristics of the obese population. The ICER varies from US$5400 per QALY in 55-year-old females with BMI of 50 to US$35,600 per QALY in 55-year-old males with a baseline BMI of 40.

Salem and colleagues[142] do not report the results across the same subgroups as Craig and Tseng,[140] which makes it impossible to compare variability of estimates of incremental cost-

TABLE 46 *Cost-effectiveness estimates of bariatric surgeries as compared to the alternative treatment strategy Jensen and Flum[141]*

Type of treatment strategies	Results: Open GBP vs non-surgical treatment		
	Incremental cost	Incremental outcome (additional LY gained)[a]	ICER
Open GBP vs diet and exercise[141]	US$4600	0.61	US$7126/QALY

GBP, gastric bypass; ICER, incremental cost-effectiveness ratio; LY, life year; QALY, quality-adjusted life-year.
a   Jensen and Flum 2005[141] do not report incremental QALYs accumulated over patients' lifetime

TABLE 47 *Cost-effectiveness estimates of bariatric surgeries as compared to the alternative treatment strategy as reported in Craig and Tseng[140] and Salem and colleagues[142]*

Subgroup	Cost of intervention (Open GBP)	Cost of comparator (non-surgical treatment)	QALY intervention[a]	QALY comparator (non-surgical treatment)	ICER
Results: Open GBP vs non-surgical treatment[140]					
Men 35 years; BMI 40	US$68,600	US$38,500	19.56	18.51	US$28,600/QALY
Men 35 years; BMI 50	US$75,000	US$53,200	18.87	16.83	US$10,700/QALY
Men 55 years; BMI 40	US$77,600	US$47,900	13.32	12.48	US$35,600/QALY
Men 55 years; BMI 50	US$85,300	US$63,500	12.81	11.17	US$13,300/QALY
Women 35 years; BMI 40	US$59,000	US$35,300	19.82	18.21	US$14,700/QALY
Women 35 years; BMI 50	US$64,800	US$48,500	18.88	16.03	US$5700/QALY
Women 55 years; BMI 40	US$69,600	US$48,200	13.94	12.62	US$16,100/QALY
Women 55 years BMI 50	US$77,000	US$64,100	13.23	10.88	US$5400/QALY
Results: LGBP vs non-surgical treatment[142]					
Men 35 years; BMI 40	US$27,560	n/r	n/r	n/r	US$18,543/QALY
Women 35 years; BMI 40	US$27,560	n/r	n/r	n/r	US$14,680/QALY
Results: LAGB vs non-surgical treatment[142]					
Men 35 years; BMI 40	US$16,200	n/r	n/r	n/r	US$11,604/QALY
Women 35 years; BMI 40	US$16,200	n/r	n/r	n/r	US$8878/QALY

BMI, body mass index; GBP, gastric bypass; ICER, incremental cost-effectiveness ratio; LAGB, laparoscopic adjustable gastric banding; LGBP, laparoscopic gastric bypass; n/r= not reported; QALY, quality-adjusted life-year.
a   QALY intervention was open GBP, LGBP or LAGB, as indicated.

effectiveness in various subgroups of the obese population. However, the authors reported that both bariatric procedures in comparison to non-surgical treatment were cost-effective at < $25,000 per QALY for all base-case scenarios (i.e. the combinations of baseline age of either 35, 45, or 55 years and BMI of either 40, 50 or 60).

Salem and colleagues[142] concluded that laparoscopic adjustable gastric banding is more cost-effective than laparoscopic gastric bypass for all base-case scenarios. However, this conclusion is based on the ICERs individually comparing

laparoscopic gastric bypass with non-surgical treatment and laparoscopic adjustable gastric banding with non-surgical treatment, whereas the direct comparison of these two surgical interventions in terms of incremental costs and QALYs was not reported. Therefore this conclusion may not be true for every subgroup of the obese population.

Sensitivity analysis

Eight one-way sensitivity analyses undertaken by van Mastrigt and colleagues[139] were undertaken

to test the sensitivity of the outcomes associated with variability of cost estimates used in CEA (with outcomes expressed in % EWL) and CUA. The cost of operating-theatre personnel time (€2.96 per minute) was substituted in turn for the maximum and minimum values of €3.56 and €2.66 per minute respectively. Also the per diem cost (€332 per day in hospital) was substituted for the maximum and minimum values of €432 and €232 per day respectively. The results reported in terms of the outcomes of bootstrapping analyses of joint distribution of incremental costs and outcomes are very robust with respect to variations in unit cost estimates. A scenario analysis from the alternative health-care system perspective (rather than the societal perspective used in the original economic evaluation) was also undertaken. With respect to the QALY outcome exclusion of non-medical costs, that represent 39% and 35% of open vertical banded gastroplasty and laparoscopic adjustable gastric banding costs, respectively, has reduced the probability of laparoscopic adjustable gastric banding being a dominant strategy (from 79% to 68%) and increased the probability of laparoscopic adjustable gastric banding being more effective and more expensive (from 14% to 27%). van Mastrigt and colleagues[139] did not test the uncertainty associated with clinical effectiveness or utility estimates observed in the RCT.

Ackroyd and colleagues[138] do not seem to test the variability in cost estimates using a sensitivity analysis. Instead the authors conducted a two-way sensitivity analysis where clinical effectiveness of laparoscopic adjustable gastric banding and laparoscopic gastric bypass with respect to both BMI reduction and Type 2 diabetes prevalence was reduced by 20% in each arm of the model, which is equivalent to assigning zero Type 2 diabetes benefits from a non-surgical treatment in the first year. The ICER for laparoscopic adjustable gastric banding compared with non-surgical treatment changed from £1929 to £3251 per QALY. The ICER for laparoscopic gastric bypass compared to non-surgical treatment changed from £1517 to £2599 per QALY. The ICERs appear to be very sensitive to variability in clinical effectiveness estimates. The sensitivity of results to the variations in utility estimates was not tested in this study.

Jensen and Flum[141] conducted a series of one-way sensitivity analyses and the outcomes are reported to be sensitive to the estimated cost of complications (although the range was not reported) and the discount rate (neither the value nor the range were reported).

Craig and Tseng[140] conducted a series of one-way sensitivity analyses that varied the short-term clinical effectiveness parameters (%EWL, mortality rates and complication rates) and the long-term outcomes (LYs lost as the result of the elevated BMI). Another sensitivity analysis was conducted to assess the impact of variability in utility estimates. However, instead of varying the utility values, the regression coefficients in the (unreported) multiple regression equation (see the section on Translation of short-term outcomes into final outcomes, this chapter) used to obtain utility values were decreased by 25%. It is not clear how the actual utility values were affected.

Two-way sensitivity analysis varying both the lifetime medical cost and the discount rate was undertaken by Craig and Tseng.[140] Another two-way sensitivity analysis varied the estimated %EWL and the reimbursement rates for the insured patients. These parameters were also used in the threshold analysis for the subgroup of insured 55-year-old men with the baseline BMI of 40 with the ICER of $50,000 per QALY as a threshold. The results indicated that under the base-case assumptions about the 67% reimbursement rate, the loss of excess weight greater than 46% is sufficient for the incremental cost per incremental QALY to be below US$50,000. The threshold analysis implicitly assumed the change of the perspective of the economic evaluation from that of the health-care system (where the cost of medical care is covered by both the third party and the patients' copayments) to the perspective of the individually insured patients. It was also implicitly assumed that for any payer (Government, the third party or an insured individual) the same criterion of value for money is applied (i.e. the threshold of $50,000 per QALY). This may not be a reasonable assumption.

Craig and Tseng[140] concluded that the results reported in Table 47 appear to be robust to all parameter variations for the subgroups of women and younger more obese men. An open gastric bypass may not be cost-effective for some subgroups of older and less obese men as the ICER exceeds US$50,000 per QALY when the base-case assumptions about some clinical effectiveness parameters are varied.

Salem and colleagues[142] investigated the uncertainty associated with parameter estimates in the model, but the source of the ranges in parameter estimates, and the methods used to derive them, were not clear. A series of one-way sensitivity analyses were performed and results

are said to be sensitive to the value of the primary clinical outcome (%EWL), cost of the surgical procedure, number of times the band adjustment was required for the laparoscopic adjustable gastric banding procedure and the estimated rate of operative mortality for laparoscopic gastric bypass.

To summarise, none of the identified studies undertook a probabilistic sensitivity analysis. The rationale for choosing the model parameters and the ranges included in the sensitivity analysis is not clear in some studies.[138,139] In other studies results of the sensitivity analyses are not fully reported.[140,141] Nevertheless, based on the reported set of one-way and two-way sensitivity analyses, the results in the identified economic evaluations of bariatric surgeries appear to be fairly robust with respect to the variation in (the tested) parameter estimates.

Summary of the results reported in economic evaluations of bariatric surgeries

As discussed in the previous sections, all identified studies[138–142] are characterised by various methodological shortcomings that undermine the validity and generalisability of the reported results. Most importantly, the natural disease progression was not explicitly modelled in terms of probabilities of obesity-related diseases. Only one study[138] has modelled a Type 2 diabetes outcome explicitly and accounted for it in the final outcomes (QALYs); however, this model is limited to the five-year horizon and has numerous methodological problems and results are only relevant to the obese population with Type 2 diabetes at the baseline. Other modelled economic evaluations[138,140–142] are based on the lifetime horizon, but do not incorporate separate differential probabilities of developing/reversing obesity-related diseases. Instead, the published estimates of life expectancy and lifetime costs for the US population categorised by age, gender and BMI (up to 37.5) were used.[144] As discussed in the section on Translation of short-term outcomes into final outcomes (this Chapter) extrapolation of the life expectancy and lifetime cost estimates to include BMI values higher than 37.5 is likely to have produced unreliable estimates. Also, the unspecified method of deriving utility estimates, which was reported by Craig and Tseng[140] and replicated in Salem and colleagues,[142] may not be of sufficient methodological rigour to produce reliable estimates of QALYs. Other assumptions also appear not to correspond to the clinical evidence. In particular, the assumptions of no

weight gain in the comparator arm[140,142] does not seem to be realistic.

It appears that none of the identified modelled economic evaluations has provided a reliable and generalisable estimate of the incremental cost-effectiveness of bariatric surgeries in comparison to a non-surgical treatment. However, some of the assumptions in the identified studies are reasonable and need to be considered in the future economic evaluations:

* differential time in gaining full benefits from the different types of bariatric surgery[139]
* differential rates of short-term mortality and morbidity associated with different types of bariatric surgery[140]
* postsurgical interventions may be required immediately after the surgery[140,141] and over the longer time interval (up to five years)[138,142]
* differential rate of regaining the lost weight over the lifetime associated with the bariatric surgery and the non-surgical treatment[141]
* differential probabilities of developing/ reversing obese-related diseases as a function of changes in BMI[140–142]
* use of utility weights that relate to the changes in BMI.[141]

To summarise, none of the identified studies undertook an economic evaluation across the entire range of bariatric surgery. All modelled economic evaluations[138–142] found the bariatric surgery evaluated to be cost-effective in comparison to non-surgical treatment, although the variability in estimates of costs and outcomes is large. The choice and the range of model parameter estimates used in the sensitivity analyses were not justified. Nevertheless, with respect to the selected parameters the results appear to be robust to parameter variations in most of the CEA. The only exception, as reported by Craig and Tseng,[140] are some subgroups of older and less obese men for whom an open gastric bypass may not be cost-effective (i.e. exceeding US$50,000 per QALY) when the base-case assumptions about some clinical effectiveness parameters are varied.

It should also be noted that numerous methodological shortcomings discussed in the previous sections are likely to have resulted in biased estimates of the incremental cost-effectiveness of bariatric surgeries in comparison with the non-surgical treatment. The head-to-head RCT of two bariatric surgical procedures,[139] although being methodologically sound, was nevertheless compromised by the discrepancies

in the baseline characteristics of the population randomised to the laparoscopic adjustable gastric banding and open vertical banded gastroplasty that resulted in the difference in the baseline utility values in two intervention groups. This difference is likely to be the major reason for the contradicting results of the CEA and CUA undertaken within this study.

Uncertainties and the source of biases within economic evaluations of bariatric surgery

Clinical evidence used to obtain the primary outcomes (weight reduction)

In all four studies the BMI values were taken from the published evidence; however, it does not appear that any study conducted a systematic literature search and evidence analysis. Two studies, Craig and Tseng[140] and Jensen and Flum,[141] used the outcomes from a single published source of evidence which may affect validity of the estimate of the differential weight loss in the alternative treatments and the generalisability of results. Generalisability of results is also impaired by the choice of evidence that applies only to a subgroup of the obese population: the population of obese patients with Type 2 diabetes as in Ackroyd and colleagues[138] and white female patients who were obese at the age of 18 with BMI > 33 (or 35) (see *Table 41*, footnote d) as in Jensen and Flum.[141]

Assumptions about the target population

Craig and Tseng[140] and Salem and colleagues[142] have assumed that the cohort of obese patients with BMI > 40 have no comorbidities at the baseline, which may not be a realistic assumption.

Assumptions about the outcomes of bariatric surgeries

Ackroyd and colleagues[138] implicitly assumed that there is no differential operative mortality and postoperative morbidity between the two surgical treatments and the non-surgical treatment comparator. This is not likely to be a realistic assumption. The same is also true with respect to the assumption of a zero weight gain over the modelled time horizon in patients in the non-surgical treatment arm in Ackroyd and

colleagues,[138] Craig and Tseng[140] and Salem and colleagues.[142]

Utility estimates

Utility estimates reported in Ackroyd and colleagues[138] were also used in Craig and Tseng[140] and Salem and colleagues.[142] However, these are not likely to be unbiased estimates of the HRQoL because of the multiple methodological shortcomings in the way they were derived from the available data. In addition, the source data relate to the general population whose health-related preferences may differ from those of the obese population.

SHTAC economic model

Statement of the decision problem and perspective for the cost-effectiveness analysis

We developed a model to estimate the cost-effectiveness of bariatric surgery comparing surgical procedures against each other and against non-surgical comparators, for a UK cohort of adults meeting the NICE criteria for bariatric surgery. The perspective of the CEA is that of the NHS and Personal Social Services (PSS).

Strategies/comparators

Interventions included in the economic model are gastric bypass and gastric banding. Surgical procedures are compared with a non-surgical comparator. For patients with morbid obesity the non-surgical comparator, as in the previous report[15] consists primarily of monitoring rather than active treatment, because NICE guidance[9] specifies that patients offered bariatric surgery should have failed to achieve (or maintain) an adequate and clinically beneficial weight loss for at least six months on all appropriate non-surgical alternatives. We assume that procedures are performed laparoscopically, where possible, but that conversion to open procedures may be required.

Methods
Summary of methods and results of economic modelling in the previous assessment report[15]

The previous assessment report[15] presented estimates of the cost-effectiveness of gastric bypass, vertical banded gastroplasty and adjustable silicone gastric banding using a simple economic

model. Surgical procedures were compared with each other, as well as a non-surgical comparator. It has not been possible to repeat all of the methodological detail of the model here. Readers are therefore encouraged to consult the original report which is freely available for download (http://www.ncchta.org/fullmono/mon612.pdf).

The model in the previous report was not developed as a state transition model. However, conceptually it contained four health states: no comorbidity, remission of comorbidity, Type 2 diabetes and death. The remission of comorbidity health state was included in the model to allow for the fact that people with Type 2 diabetes may revert to normoglycaemia following successful treatment for obesity. Comorbidities other than Type 2 diabetes, such as myocardial infarction, angina and stroke, were not included. The model was used to extrapolate long-term outcomes (in terms of QALYs up to 20 years following surgery) and lifetime costs (in terms of costs of managing diabetes in addition to intervention costs) based on intermediate outcomes reported in the clinical effectiveness review (per cent weight reduction, operative mortality, percentage of people with Type 2 diabetes reverting to normoglycaemia, diabetes incidence in surgical and non-surgical patients).

In the model it was assumed that weight reduction (36% with gastric bypass, 25% to 17% for vertical banded gastroplasty, 20% to 33% with adjustable silicone gastric banding) occurred over five years following surgery, but that patients then reverted to their baseline weight of 135 kg. Operative mortality was based on a combination of trial evidence and expert opinion and was assumed to be 1% for gastric bypass, 0.5% for vertical banded gastroplasty and 0% for adjustable silicone gastric banding. Baseline diabetes prevalence in the model was 10%. Based on evidence from the Adelaide study[149] it was assumed that 75% of people with diabetes revert to normoglycaemia and remain off medication for eight years (based on follow-up from the SOS study[89,90]) – after eight years these patients revert to medication. Different diabetes incidence rates were applied to surgical and non-surgical patients (2.3% per annum for non-surgical and 0.45% per annum for surgical patients) based on data from the SOS study[89,90] – after eight years surgical patients revert to the incidence rate for non-surgical patients. Reversion to normoglycaemia and incidence rates were applied on the basis of whether patients had or had not undergone surgery and were not directly related to their weight loss or assumed BMI.

HRQoL in the model was entirely dependent on BMI (using data from an unpublished study). There were no adjustments to these utility values for patients who developed Type 2 diabetes or for people with Type 2 diabetes who reverted to normoglycaemia.

Intervention costs for non-surgical management consisted of primary-care and dietitian contacts, with a VLCD (for 12 weeks) every three years. This continued for all patients for the model time horizon. Intervention costs for surgery consisted of preoperative assessment (including outpatient and dietitian appointments as well as psychological assessment), surgery (based on theatre time, length of ward stay, admission to an ITU or high-dependency unit (HDU), and percentage of reoperations) and postdischarge management (consisting of outpatient follow-up, community dietitian contacts, psychology consultations and primary care). Disease management costs in the model were limited to those associated with diabetes, using the assumptions on diabetes prevalence, reversion to normoglycaemia and diabetes incidence for surgical and non-surgical patients described earlier. Annual cost per person with Type 2 diabetes was taken from the CODE-2 study.[160]

The model had a 20-year time horizon and the analysis adopted the perspective of the NHS and personal social services. The baseline cohort in the model was 90% female, had an average age of 40, average body weight of 135 kg and an average BMI of 45. The baseline model assumed no change in life expectancy and only included postoperative mortality; all-cause or disease-specific mortality was not included in the model.

Table 48 reports the base-case cost-effectiveness estimates from the previous report.[15] On the basis of these results the report concluded that surgery was a cost-effective alternative to non-surgical management and that gastric bypass may be the preferred option. The conclusion, that surgery was cost-effective was robust to changes in a series of scenario analyses. However, the report cautioned against interpreting these results as conclusive given limited data available for some of the surgical options.

Summary of findings of current review and implications for economic model
This update has identified:

- The model developed for the previous assessment report[15] based QoL entirely on

TABLE 48 *Base case from previous report[15]*

		Intervention		
		VBG	**AGB**	**GBP**
Comparator	Non-surgical	£2663; 0.26 QALY; £10237	£3831; 0.45 QALY; £8527	£2800; 0.45 QALY; £6289
	Vertical banded gastroplasty			
	Adjustable silicone gastric band	£1168; 0.19 QALY; £6,176		
	Gastric bypass	£137; 0.19 QALY; £742	£1031; 0.004 QALY; £256,856	

AGB, adjustable silicone gastric banding; GBP, gastric bypass; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; VBG, vertical banded gastroplasty;
Results are presented for each intervention (columns in table) relative to comparators (row in table) with incremental cost in the first line of each cell, incremental QALY on the second line of each cell and the ICER (incremental cost per QALY gained) on the bottom line of each cell.

BMI and took no account of the effect of comorbidity on QoL. Since the publication of the previous assessment report[15] a systematic review on patient utilities related to body weight and a number of additional models has been published, in some cases suggesting a larger reduction in QoL in relation to BMI. For this report we intend adopting an estimate of the impact of BMI on utility, and including additional state-specific utility decrements for patients experiencing comorbidities (Type 2 diabetes and CVD).

- The model developed for the previous assessment report[15] included Type 2 diabetes as the only comorbidity of obesity. This was based on evidence from included studies that weight loss following bariatric surgery was associated with:
  - reversion to normoglycaemia or cessation of medication for patients with pre-existing Type 2 diabetes;[89,149,161]
  - reduced incidence of diabetes [0% versus 4.7% at two years (corresponding to annual incidence of 0% versus 2.41% using the declining exponential approximation to life expectancy, or DEALE, method[162]) and 3.6% versus 18.5% at eight years (corresponding to annual incidence of 0.45% versus 2.56% using the DEALE method) for surgical and control patients respectively];[89]
  - transient effect on hypertension.[89,149,161]
- Adopting a deliberately conservative approach the previous review limited the scope of comorbidities considered to Type 2 diabetes. As discussed earlier, the impact of Type 2 diabetes

was limited to the cost impact, no estimate of the impact on QoL was included in the model.

For the analysis in this report we adopt a set of BMI-specific Type 2 diabetes incidence estimates and include estimates of cardiovascular comorbidities, where trial data support such estimates (see section on Data sources, Effectiveness data, this chapter, for details and discussion).

- Costings developed for the previous assessment report[15] were predominantly based on expert opinion, in terms of preoperative assessments, surgical costs and postdischarge management. Since the publication of the previous assessment report[15] a number of economic evaluations have been published reporting costs or resource use assumptions for different types of bariatric surgery. For this report we intend updating the cost assumptions in relation to bariatric surgery, where published evidence or expert opinion suggests there have been substantial changes since the publication of the previous assessment report.[15]
- Methodological guidance and accepted practice in discounting have changed since the publication of the previous assessment report,[15] where costs and outcomes were each discounted at 6%. Updated estimates, using the original model, are presented in Appendix 18 using the current practice of discounting both costs and outcomes each at 3.5%. Where this has a substantial impact on the results of the analysis, this will be discussed in the conclusions of this report.

Model type and rationale for the model structure

For this report we have sought to expand the conceptual model adopted for the previous assessment report, to include CHD and stroke. *Figure 2* shows the state transition diagram for the model developed for this review. In this diagram ellipses indicate health states and arrows indicate allowable transitions. Patients may enter the model in any of the grey-shaded ellipses – i.e. they may have already developed Type 2 diabetes as a result of their obesity, they may resolve diabetes (temporarily or permanently) as a result of treatment for their obesity or they may enter the model free of diabetes. We assume that patients are free of CHD and have not experienced stroke before treatment.

The primary outcomes reported for clinical trials included in this review are typically related to change in body weight (total weight change from baseline, change in excess weight or change in BMI) so data to model transitions between health states would ideally be based on a standardised, weight-related measure such as BMI. However, body weight may not be an ideal parameter for predicting some comorbidities associated with obesity – for example, CHD and stroke are more

typically modelled using blood pressure and lipid measurements rather than BMI. The reporting of these additional measures is not complete in all studies. Where these additional parameters are not available in trial reports it may not be possible to apply the full model described before – in that situation a more limited model, similar to that adopted for the previous report will be used.

The models have a maximum time horizon of 20 years, as adopted in the previous assessment report, to allow for some extrapolation of trends in weight loss beyond the end of trial follow-up. This time horizon represents a trade-off between allowing the benefits of continued weight reduction (compared with baseline) to accrue and the limited long-term follow-up data, uncertainty over its applicability to current clinical practice and surgical technology (including the absence of reliable data on long-term reoperation rates and conversions). In the analyses conducted using the updated model cost-effectiveness results are presented for three time horizons – trial-only (two years), intermediate extrapolation (to five years) and a longer term extrapolation (to 20 years). The purpose of this is to identify how far the extrapolation of benefits, beyond the trial period, affects the cost-effectiveness estimates.
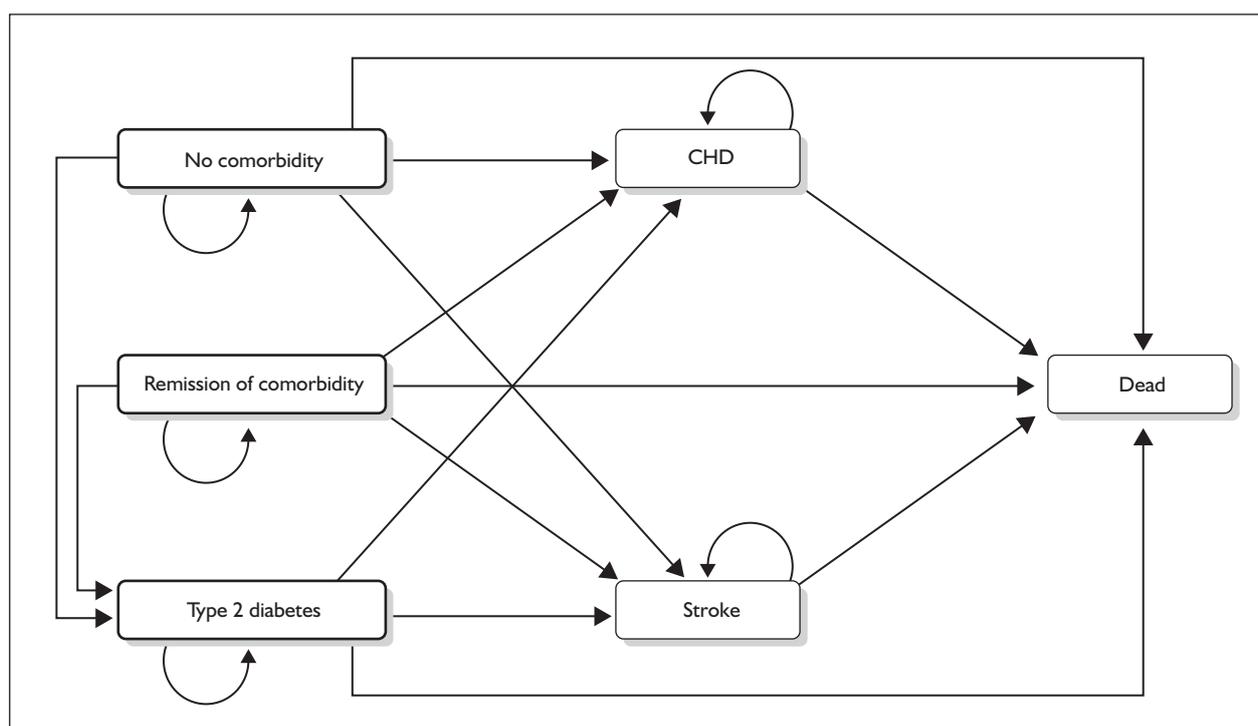
FIGURE 2 *State transition diagram. CHD, coronary heart disease.*

Baseline cohort of patients with morbid obesity

The baseline cohort consists of patients with morbid obesity, with a BMI of 45, 90% of which are female, with a mean age of 40, and all have failed to achieve or maintain adequate, clinically beneficial weight loss for at least six months using appropriate non-surgical measures. This is similar to the baseline cohort for the previous report and is consistent with current NICE guidance.[9] It is estimated that 10% of morbidly obese patients, eligible for treatment, have Type 2 diabetes before the start of treatment with surgical or non-surgical treatment to promote weight loss.

Additional analyses will be undertaken for a cohort of obese patients, mean BMI of 37 with Type 2 diabetes (adopting the baseline characteristics of the trial reported by Dixon and colleagues[117]). Treatment outcomes from the trial reported by Dixon and colleagues[107] will be applied to estimate the cost-effectiveness of bariatric surgery in this group of patients. These patients meet the NICE criteria in having a BMI greater than 35 and other significant disease (Type 2 diabetes) that could be improved if they lost weight. However, it is not clear from the trial report whether these patients had previously failed to achieve or maintain weight loss with non-surgical interventions. Analyses will also be presented based on characteristics and clinical outcomes for patients recruited to the trial reported by O'Brien and colleagues,[115] which selected patients with moderate obesity (baseline BMI between 30 and 35) and are therefore outside the scope of the NICE guideline.

Data sources

Effectiveness data

Effectiveness – percentage weight reduction

We have reported on the findings from our systematic review on the clinical effectiveness of bariatric surgery (see Chapter 4, Assessment of clinical effectiveness evidence) and also the findings of the review of natural history models and clinical effectiveness data used in economic evaluations of interventions included in this report (Results, this chapter). The clinical effectiveness review concluded that it was not appropriate to conduct a meta-analysis because of the limited number of studies for comparison of surgical procedures, differences in surgical and non-surgical comparators, heterogeneity of patient populations, and poor reporting (no reporting of standard deviations or equivalent measures of variation). In the absence of formally analysed, robust estimates of the relative effectiveness of surgical and non-

surgical approaches, based on all relevant studies included in the clinical effectiveness review, the effectiveness data for this economic evaluation have been derived from five sources:

1. effectiveness estimates adopted in the previous assessment report[15]
2. a prospective randomised trial of laparoscopic adjustable gastric banding and laparoscopic Roux-en-Y gastric bypass[107]
3. an RCT of laparoscopic adjustable gastric banding and conventional therapy for patients with BMI of greater than 30 and less than 40, with Type 2 diabetes[117]
4. an RCT of laparoscopic adjustable gastric banding and an intensive medical programme for patients with BMI of greater than 30 and less than 35[115]
5. trends in weight reduction for surgical patients and non-surgical controls, over 10 years, from the SOS study.[97]

Percentage weight reduction in morbidly obese subjects[15,97,107]

The previous assessment report estimated a percentage weight reduction for bariatric surgery procedures separately, with an underlying assumption that long-term weight loss was very unlikely to occur in patients undergoing non-surgical management, based on data from the SOS study. The baseline assumption for Roux-en-Y gastric bypass, on the basis of a visual inspection of the percentage weight loss from baseline in eight studies, was that patients lose 36% of initial weight and that this weight loss is maintained for five years following surgery. There was more limited evidence on weight reduction following adjustable gastric banding – the baseline assumption corresponded to the percentage weight loss reported in an RCT of adjustable gastric banding and vertical banded gastroplasty.[126]

Table 49 reports the baseline weight (or BMI where weight reduction was not reported) for included trials of gastric bypass and the absolute change in weight or BMI reported for each year of follow-up in the trial.

Table 50 reports the percentage weight reduction (or percentage reduction in BMI where weight reduction was not reported) calculated from the values reported in *Table 49*. The baseline assumption of a 36% reduction in weight for gastric bypass, adopted in the previous assessment report, is at the upper extreme of the values reported in *Table 50*.

TABLE 49 *Absolute weight reduction and reduction in BMI following gastric bypass, reported in included studies*

Study	Baseline	Year 1	Year 2	Year 3	Year 4	Year 5
Absolute weight reduction (kg)						
Howard[120]	154	55	53	54		50
Sugerman[123]	132	44	44	41		
Angrisani[107]	118	25		35		34
Absolute reduction in BMI (kg/m²)						
Stoeckli[102]	43.6		10.7			
Olbers[108]	42.7	13.7	14.7			
Lee[124]	43.18	13.6	14.7			
BMI, body mass index.						

For consistency, the percentage weight reduction adopted in the previous report will be used in this evaluation – these represent the most optimistic assumptions for weight reduction following gastric bypass. A second set of effectiveness estimates, based on percentage weight reduction reported by Angrisani and colleagues,[107] will also be reported. These represent the least optimistic assumptions for weight reduction following gastric bypass.

Table 51 reports the baseline weight (or BMI where weight reduction was not reported) for included trials of adjustable gastric banding and the absolute change in weight or BMI reported for each year of follow-up in the trial.

Table 52 reports the percentage weight reduction (or percentage reduction in BMI where weight reduction was not reported) calculated from values reported in *Table 51*. The baseline assumption of an initial 20% reduction in weight in the first year rising to a 33% weight reduction at

five years, adopted in the previous assessment report, is the most optimistic set of assumptions for weight reduction following adjustable gastric banding and contrasts starkly with the results of the trial reported by Angrisani and colleagues.[107] For consistency the percentage weight reduction adopted in the previous report will be used in this evaluation. However a second set of effectiveness estimates, based on percentage weight reduction reported by Angrisani and colleagues[107] will also be reported, representing the least optimistic assumptions for weight reduction following adjustable gastric banding.

Data on trends in weight reduction for surgical patients and non-surgical controls, over 10 years, from the SOS study[97] are used to extrapolate beyond five years of follow-up. Percentage weight reduction for gastric bypass patients was estimated to decline by 17.7% from five to 10 years of follow-up (estimated from Sjostrom and colleagues[97], see Figure 1 of their article). The equivalent decline for

TABLE 50 *Per cent weight reduction and percentage reduction in BMI following gastric bypass, reported in included studies*

Study	Year 1	Year 2	Year 3	Year 4	Year 5
Percentage weight reduction					
Howard[120]	36%	34%	35%		32%
Sugerman[123]	33%	33%	31%		
Angrisani[107]	21%		29%		29%
Percentage reduction in BMI					
Stoeckli[102]		25%			
Olbers[108]	32%	34%			
Lee[124]	31%	34%			
BMI, body mass index.					

TABLE 51 *Absolute weight reduction and reduction in BMI following adjustable gastric banding, reported in included studies*

Study	Baseline	Year 1	Year 2	Year 3	Year 4	Year 5
Absolute weight reduction (kg)						
Angrisani[107]	117	15		19		19
Nilsell[126]	124	26	36	39	38	43
De Wit[132]	152	35				
Absolute reduction in BMI (kg/m²)						
Stoeckli[102]	41.7	8.0	8.5			
Morino[110]	44.7	9.2	9.9	9.0		
Van Dielen[127]	46.7	11.7	12.1			
BMI, body mass index.						

adjustable gastric banding patients was estimated to be 14.7%.

Table 53 reports the percentage weight reduction applied in the model for each intervention and comparator for morbidly obese patients. Where values were not reported for each year (Angrisani and colleagues reported trial outcomes at year 1, year 3 and year 5) values were estimated by linear interpolation.

Percentage weight reduction in obese subjects with Type 2 diabetes[117]
Table 54 reports the weight loss from baseline for patients followed up for two years following surgery using laparoscopic adjustable gastric banding compared with conventional diabetes care with a focus on weight loss by lifestyle change in the trial reported by Dixon and colleagues.[117]

For the base-case analysis it is assumed that the reduction in BMI occurs from entry to the study

and persists for two years with reversion to baseline BMI of 37 kg/m² at the end of the study period (two years). An additional analysis will be reported, extrapolating the percentage weight reduction over 10 years using data on trends in weight reduction for patients undergoing gastric banding from the SOS study,[97] which suggest that the percentage weight reduction from baseline reduces by one-third from two to 10 years following surgery.

Percentage weight reduction in moderately obese subjects[115]
Table 55 reports the percentage weight loss from baseline at four observation points for moderately obese patients followed up for two years following surgery using laparoscopic adjustable gastric banding compared with a non-surgical programme using behaviour modification, VLCDs and pharmacotherapy.

For the base-case analysis it is assumed that the reduction in BMI follows the pattern described by

TABLE 52 *Percent weight reduction and percentage reduction in BMI following adjustable gastric banding, reported in included studies*

Study	Year 1	Year 2	Year 3	Year 4	Year 5
Percentage weight reduction					
Angrisani[107]	13%		16%		16%
Nilsell[126]	21%	29%	31%	31%	35%
De Wit[132]	23%				
Percentage reduction in BMI					
Stoeckli[102]	19%	20%			
Morino[110]	21%	22%	20%		
Van Dielen[127]	25%	26%			
BMI, body mass index.					

TABLE 53 *Percentage weight reduction over ten years for morbidly obese patients undergoing non-surgical or surgical management, applied in the base-case economic model*

Time (years)	Non-surgical management	Gastric bypass		Adjustable gastric banding	
		Optimistic	Pessimistic	Optimistic	Pessimistic
0	0.0	0.0	0.0	0.0	0.0
1	0.0	−36.0	−21.4	−21.0	−12.6
2	0.0	−36.0	−25.3	−29.0	−14.4
3	0.0	−36.0	−29.2	−31.5	−16.2
4	0.0	−36.0	−29.0	−30.6	−16.3
5	0.0	−36.0	−28.8	−34.7	−16.4
6	0.0	−34.7	−27.8	−33.7	−15.9
7	0.0	−33.5	−26.8	−32.6	−15.4
8	0.0	−32.2	−25.8	−31.6	−15.0
9	0.0	−30.9	−24.7	−30.6	−14.5
10	0.0	−29.6	−23.7	−29.6	−14.0

Gastric bypass
Optimistic values from one to five years are taken from the previous assessment report. Percentage weight loss at 10 years is based on 17.7% decline in percentage weight loss observed from five to 10 years in the SOS study.[97] Values between five and 10 years estimated by linear interpolation.
Pessimistic values from one to five years are taken from Angrisani and colleagues.[107] Values for two and four years were not reported and are estimated by linear interpolation. Percentage weight loss at 10 years is based on 17.7% decline in percentage weight loss observed from five to 10 years in the SOS study.[97] Values between five and 10 years estimated by linear interpolation

Adjustable gastric banding
Optimistic values from one to five years are taken from Nilsell and colleagues[126]. Percentage weight loss at 10 years is based on 14.7% decline in percentage weight loss observed from five to 10 years in the SOS study.[97] Values between five and 10 years estimated by linear interpolation.
Pessimistic values from one to five years are taken from Angrisani and colleagues.[107] Values for two and four years were not reported and are estimated by linear interpolation. Percentage weight loss at 10 years is based on 14.7% decline in percentage weight loss observed from five to 10 years in the SOS study.[97] Values between five and 10 years estimated by linear interpolation

the solid lines in *Figure 3*, showing the estimated BMI over time for surgical and non-surgical cohorts. This figure reproduces Figure 3 from the original trial report[115] except that it plots estimated BMI (reported in *Table 54*), rather than per cent weight loss from baseline. For the base-case analysis both cohorts revert to baseline BMI at the end of two years, i.e. applying data from the clinical trial report with no extrapolation of effect beyond the trial duration. Inspection of *Figure 3* suggests

that BMI for the non-surgical cohort is already reverting toward the baseline level at two years, whereas for the surgical cohort the BMI appears to be stabilising around a value 20% below the baseline level.

An additional scenario is considered:

*   As illustrated using the dashed lines in *Figure 3*, a linear extrapolation has been estimated using the final two BMI values (month 18 and month 24) for the non-surgical cohort. This suggests that BMI is reverting to its baseline value at a rate of 0.106 points per month. On this basis the estimated BMI reverts to its baseline value 18 months after the end of the two-year study period. Applying the same rate of increase for the surgical cohort implies that BMI reverts to its baseline value 68 months ($5^2/_3$ years) after the end of the two-year study period.

TABLE 54 *Absolute weight loss and estimated BMI, from a baseline BMI of 37, for obese subjects with Type 2 diabetes[117]*

Intervention	Weight loss (standard error)	BMI
Surgical	21.1 (1.9170)	29.6
Non-surgical	1.5 (0.9859)	36.6

BMI, body mass index.

TABLE 55 *Percentage weight loss and estimated BMI, from a baseline BMI of 33.5 kg/m2, for moderately obese subjects[115]*

Intervention	6 months		12 months		18 months		24 months	
	Weight loss (%)	BMI	Weight loss (%)	BMI	Weight loss (%)	BMI	Weight loss (%)	BMI
Surgical	14.1	28.8	19.7	26.9	20.8	26.5	21.6	26.3
Non-surgical	13.9	28.8	10.0	30.1	7.5	31.0	5.6	31.6

BMI, body mass index.
BMI has been estimated using the percentage weight loss from baseline, reported in the previous column, against a baseline BMI of 33.5 kg/m^2

Effectiveness – diabetes resolution

The previous assessment report estimated the proportion of morbidly obese patients with existing Type 2 diabetes who revert to normoglycaemia following bariatric surgery as 75%, based on the proportion of patients who were off medication at three years reported by Hall and colleagues.[149] Similar proportions have been reported for patients with Type 2 diabetes in the SOS study (72% recovery from diabetes at two years)[97] and Dixon and colleagues[117] (73% remission of diabetes in surgical patients versus 13% in conventionally treated patients, though these were patients with a lower BMI of between 30 and 40). At 10 years of follow-up the SOS study[97] reported that 36% of patients who had had Type 2 diabetes at baseline, were in remission following bariatric surgery. For the base case we adopt the assumption that 75% of prevalent Type 2 diabetes cases revert to normoglycaemia up to two years

following bariatric surgery and that 36% are in recovery at 10 years – the percentage of patients for intermediate years is estimated using linear interpolation. The proportion of patients in the control cohort in the SOS study[97] is used to estimate recovery from Type 2 diabetes with non-surgical management. These values are 21% at two years and 13% at 10 years – as with the surgically managed patients the values for intermediate years are estimated using linear interpolation.

Diabetes resolution in obese subjects with Type 2 diabetes[117]

Table 56 reports the percentage of patients with Type 2 diabetes at baseline, who were in remission at two years following surgery using laparoscopic adjustable gastric banding compared with conventional diabetes care in the trial reported by Dixon and colleagues.[117]
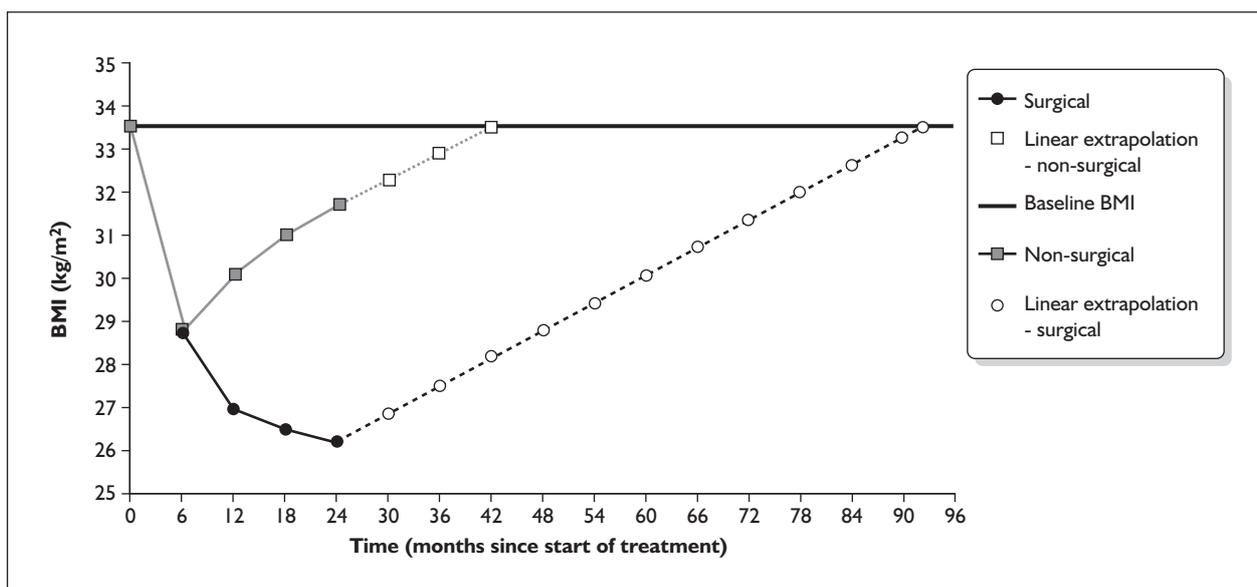
FIGURE 3 *Estimated BMI for moderately obese subjects over two years surgical and non-surgical treatment. BMI, body mass index.*

TABLE 56 *Percentage of obese subjects with Type 2 diabetes patients resolving diabetes[117]*

Intervention	Per cent of patients resolving diabetes (standard error)
Surgical	73.3 (0.0811)
Non-surgical	13.3 (0.0614)

For the base-case analysis it is assumed that the resolution of diabetes occurs from entry to the study and persists for two years with reversion to Type 2 diabetes at the end of the study period (two years).

Effectiveness – change in blood pressure and lipids
The effect of bariatric surgery on blood pressure and lipids is not included in the model for morbidly obese patients because the baseline ratio of total to HDL-cholesterol and change from baseline over time was not reported in any of the included studies. Hence the model for morbidly obese patients does not include an estimate of the effect of bariatric surgery on cardiovascular morbidity or mortality.

Change in blood pressure and lipids in obese subjects with Type 2 diabetes[117]
Table 57 reports the change in systolic blood pressure and change in the ratio of total to HDL-cholesterol from baseline for patients followed up for two years following surgery using laparoscopic adjustable gastric banding compared with conventional diabetes care in the trial reported by Dixon and colleagues.[117]

For the base-case analysis it is assumed that the change in systolic blood pressure (from a baseline value of 135 mmHg) and change in ratio of total to HDL-cholesterol (from a baseline ratio of 4.4) occurs from entry to the study and persists for two years with reversion to baseline values at the end of the study period (two years).

Change in blood pressure and lipids in moderately obese subjects[115]
Table 58 reports the change in systolic blood pressure and change in the ratio of total to HDL-cholesterol from baseline at four observation points for moderately obese patients followed up for two years following surgery using laparoscopic adjustable gastric banding compared with a non-surgical programme using behaviour modification, VLCDs and pharmacotherapy.

For the base-case analysis it is assumed that the change in systolic blood pressure (from a baseline of 131 mmHg) and change in ratio of total to HDL-cholesterol (from a baseline ratio of 4.3) occurs from entry to the study and persists for two years with reversion to baseline values at the end of the study period (two years). For the alternative scenarios – where reduction in BMI below baseline levels is assumed to persist beyond two years (up to 18 months for non-surgical and 68 months for the surgical cohort in the first scenario, and up to 14 months for the second) – the same duration of effect is assumed for changes in systolic blood pressure and ratio of total to HDL-cholesterol. Values between the observed changes at two years and the assumed date of reversion to baseline are estimated by linear interpolation.

Diabetes incidence by BMI
The Description of health problem section in chapter 1 of this report briefly reviewed epidemiological evidence for the association between BMI and Type 2 diabetes, indicating an approximate doubling of the odds of Type 2 diabetes for obese subjects compared with those with a BMI less than 25. Targeted searches were undertaken to identify studies reporting diabetes incidence by BMI. Economic evaluations of interventions to promote weight reduction were also identified and searched for data relating BMI and diabetes incidence.

TABLE 57 *Change in systolic blood pressure, from a baseline of 135 mmHg, and change in the ratio of total to HDL-cholesterol, from a baseline ratio of 4.4, for obese subjects with Type 2 diabetes[107]*

Intervention	Change in systolic blood pressure, mmHg (standard error)	Change in the ratio of total to HDL-cholesterol (standard error)
Surgical	−6.0 (3.2681)	−0.82 (0.3469)
Non-surgical	−1.7 (2.5926)	−0.14 (0.1899)
HDL, high-density lipoprotein.		

TABLE 58 *Change in systolic blood pressure, from a baseline of 131 mmHg, and change in the ratio of total to HDL-cholesterol, from a baseline ratio of 4.3, for obese subjects with Type 2 diabetes*[115]

Intervention	Change in systolic blood pressure % (standard error)	Change in the ratio of total to HDL-cholesterol % (standard error)
Surgical	−10.8 (1.7294)	−21.3 (2.4019)
Non-surgical	−7.2 (1.7422)	−8.0 (2.8198)
HDL, high-density lipoprotein.		

Column two of *Table 59* reports estimates of diabetes incidence by BMI, derived by Warren and colleagues.[163] These are based on data reported by Colditz and colleagues[164] (column one *Table 59*), which reported diabetes incidence by bounded categories, up to a BMI value of 34.9, with the final incidence rate applied to an unbounded BMI category of 35 and over. Warren and colleagues[163] extrapolated for values beyond 35 kg/m² using data from Sjostrom and colleagues,[88] which reported two-year incidence in control patients (who did not lose weight and had average BMI of 40) of 6.3% versus a diabetes incidence of 0.2% in treated patients, who achieved an average weight reduction of 27.8 kg (reducing average BMI from 42.1 to 32.4 kg/m²).

Comparing the incidence rates estimated by Warren and colleagues[163] with those adopted in the previous report [2.3% without surgery (BMI of 45) and 0.45% with surgery (BMI between 29 and 38)] suggests that adopting these BMI-specific values would estimate a greater difference in diabetes incidence than would be the case with the original model. For example, the original model predicted that, in cohorts of 100 patients with an initial BMI of 45, an initial Type 2 diabetes prevalence of 10%, and a reduction in BMI of 16 points (over five years) following surgery compared with no reduction for non-surgical management, 43% treated non-surgically and 35% treated with gastric bypass would have Type 2 diabetes after 20 years. The equivalent values using the same baseline assumptions as in the original model, but using the BMI-specific incidences, are 53% and 41% respectively. The difference in diabetes incidence between the two cohorts is therefore 9% in the original model and 12% using the incidence rates adopted by Warren and colleagues.[163]

An alternative method for estimating BMI-specific diabetes incidence for values of BMI beyond 35 would be to fit a regression line. *Table 59* reports the results of fitting a polynomial regression, using the mid-points of the BMI categories, to the age-standardised incidences for the bounded categories

up to 34.9. The regression equation is then used to extrapolate values beyond BMI of 35. This gives an estimated incidence of 2.5% for a BMI of 45, which is more consistent with values adopted for the model used in the previous report.[15] Repeating the comparison described earlier, in cohorts of 100 patients with an initial BMI of 45, an initial Type 2 diabetes prevalence of 10%, and a reduction in BMI of 16 points (over five years) following surgery compared with no reduction for non-surgical management, 46% treated non-surgically and 36% treated with gastric bypass would have Type 2 diabetes after 20 years. The difference in diabetes incidence between the two cohorts is therefore 9% in the original model and 10% using the polynomial regression for extrapolation.

We adopt the extrapolation based on the polynomial regression for the base case in the model, applying the values estimated by Warren and colleagues[163] in a sensitivity analysis.

Coronary heart disease
Targeted searches failed to find reliable published estimates relating CHD [acute myocardial infarction (AMI) or angina] to BMI alone. Where data were identified they related to CHD mortality[165–167] rather than incidence or CHD events and used BMI categories that were of little benefit in populating the model (e.g. upper BMI categories set at greater than or equal to 32 or greater than or equal to 35).

To estimate CHD for patients with and without diabetes the Framingham Heart Study (FHS) accelerated failure time risk equations are used,[168] which predict first cardiovascular events. The hazard of CHD events is estimated based on sex, age, systolic blood pressure, smoking status, total cholesterol to HDL-cholesterol ratio (TC:HDL). These equations are typically used to derive 10-year risks. However, a reparameterisation, as proposed by Caro and colleagues[169] has been adopted to estimate hazards for each model cycle (see Appendix 19 for details).

TABLE 59 *Diabetes incidence by BMI*

BMI	Colditz and colleagues[164] Age standardised risk per 100,000 persons	Warren and colleagues[163] % annual incidence	Polynomial regression using estimates of Colditz and colleagues[164]
22–22.9	37.4	0.04	0.04
23–23.9	54.9	0.05	0.05
24–24.9	62.9	0.06	0.07
25–26.9	103.5	0.10	0.11
27–28.9	200.4	0.20	0.21
29–30.9	354.5	0.35	0.34
31–32.9	521.2	0.52	0.51
33–34.9	703.6	0.70	0.71
35–36.9	1190.5[a]	1.19	0.95
37–38.9		1.55	1.23
39–40.9		2.00	1.55
41–42.9		2.50	1.90
43–44.9		3.15	2.28

BMI, body mass index.
Polynomial regression diabetes incidence $= 2.18627 - (0.19792 \times BMI) + (0.00455 \times BMI^2)$
a   This value applied to the group of individuals with BMI ≥ 35 in the study reported by Colditz and colleagues and is therefore likely to overestimate the incidence for the group with BMI 35 to 36.9, although this is taken as the rate for that category by Warren and colleagues[163]

The Framingham equation for myocardial infarction only, is used in the model, therefore the model does not predict angina in the modelled cohorts.

To apply the FHS risk equations, information on baseline systolic blood pressure and TC:HDL and also changes from baseline are required for included clinical trials. These data are not available for all trials and therefore predictions of CHD risk may not be available for all comparisons. In that situation a more limited version of the model, similar to that adopted for the previous report,[15] will be used.

Stroke
Targeted searches identified studies describing associations between total stroke risk (also broken down by ischaemic and haemorrhagic stroke) by BMI for both men[170] and women.[171] Both studies found significantly higher stroke risk for participants with greater BMI. The relative risk was 2.00 (95% CI 1.48 to 2.71) for total stroke, 1.95 (95% CI 1.398 to 2.72) for ischaemic stroke and 2.25 (95% CI 1.01 to 5.01) for haemorrhagic stroke in men with BMI of 30 or more compared with those with a BMI less than 23. In women the relative risks of ischaemic stroke were 1.75 (95%

CI 1.17 to 2.59) for BMI of 27 to 28.9, 1.90 (95% CI 1.28 to 2.82) for BMI of 29 to 31.9 and 2.37 (95% CI 1.60 to 3.50) for BMI of 32 or more, compared with those with a BMI less than 21. For haemorrhagic stroke, in women, there was a non-significant inverse association between risk and obesity. However, as with studies reporting associations between BMI and CHD mortality, the BMI categories reported in these studies were of little benefit in populating the model (e.g. upper BMI categories set at greater than or equal to 30 or greater than or equal to 32). In addition, the reported relative risks did not distinguish between subjects with or without diabetes.

As for CHD, stroke risk for patients with and without diabetes will be estimated using the FHS risk equations,[168] which predict first stroke events, based on sex, age, systolic blood pressure, smoking status and TC:HDL. The same reparameterisation, as adopted for CHD, will be used for predicting stroke risk. However, there is no adjustment for BMI applied in calculating the stroke risks.

As discussed earlier, where baseline systolic blood pressure and TC:HDL and also changes from baseline are not reported for the included clinical trials these risks cannot be computed and a more

limited version of the model, similar to that adopted for the previous report,[15] will be used.

Health state values/utilities

A targeted search was conducted to identify published utility estimates for the BMI values relevant to the obese population included in the models. The search aimed to identify estimates of the change in utility scores based on the unit change in BMI values. Utility estimates were only considered where they used a validated, multiattribute utility scale (e.g. EQ-5D) or appropriate methodology (e.g. standard gamble or time trade-off techniques) and provided a clear definition of utility scores anchors 0 and 1 (*Table 60*). Utility values within a broader scope than is relevant to the current economic model can be found in a recent systematic review of the impact of body weight on patient utilities with or without Type 2 diabetes.[172] This systematic review does not include utility estimates associated with specific surgical interventions. Critical appraisal of utility estimates used in economic evaluations of bariatric surgeries is presented in the Translation of short-term outcomes into final outcomes section in this chapter. A systematic review of published utility estimates in the obese population,[173] published in 2004, identified only one study that assessed the change in utility scores as a function of change in BMI.[152] This study is described below.

Some of the identified studies indicated that obesity is an independent predictor of the health-related preferences with the utility scores as a function of BMI decreasing (in absolute values) as the number of covariates included in the model increases.[174,175] The search failed to identify the change in utility values specific to an obese population with CHD. However, some studies estimated the change in utility scores in obese populations with and without diabetes.[152,179] For example, Hakim and colleagues[152] found that a one-unit decrease in BMI, over a period of one year, was associated with a gain of 0.017, which was independent of age or gender. However, overweight patients with Type 2 diabetes appear to have the greatest gain in utility for a given change in BMI over one year (0.0285).

There is a large variation in the estimated change in utility with the unit change in BMI. This is likely to relate to the differences in characteristics of the population and the number of covariates included in the analysis. Recent cost-effectiveness studies in obesity[141,176] have employed the utility values reported by Hakim and colleagues[152] as these are

derived from the obese (rather than overweight) population, have a time-frame of one year (which is consistent with the typical cycle duration used in the model) and explicitly control for baseline utility values. The disadvantage of these values is that the assumption of the linear relationship between the change in utility and the change in BMI may have produced biased estimates of utility gain over the range of extreme BMI values.

We adopt the values reported by Hakim and colleagues[152] in this report, as they represent the most methodologically sound estimates derived from subjects across a wide range of obesity levels. The sensitivity of cost-effectiveness estimates to alternative assumptions regarding health-state utility is tested in a sensitivity analysis.

Cost data

Costs in the model were developed in two stages. First the additional resource use, in terms of preoperative assessments, hospital admissions for surgery, managing adverse events and postdischarge care were identified based on estimates developed for the previous review,[15] published literature, discussion with surgical specialists and a costing developed for Aberdeen specialist obesity services (U. Kulkarni, NHS Grampian, 2008, personal communication). Resource use associated with non-surgical interventions was estimated using a similar approach. The resource use estimates were combined with unit costs provided by the finance department at Southampton University Hospital Trust, and from routine published sources,[177] to provide estimates of the costs of surgical and non-surgical weight loss programmes. These are described below as intervention costs. Second, literature describing the costs of health states associated with obesity was reviewed and appropriate estimates, applicable to the UK setting, were extracted and used in the analysis. These are described below as health-state costs.

Intervention costs

Resource use associated with bariatric surgery procedures has been estimated based on estimates developed for the previous review,[15] duration of operative procedures and total length of stay used in published economic evaluations, in addition to clinical studies reviewed in Chapter 4, Assessment of clinical effectiveness evidence and discussion with surgical specialists. These are reported in *Table 61*. In the base case we estimate costs for each procedure assuming that they will be conducted laparoscopically wherever possible, using the

TABLE 60 *Change in utility values associated with a unit change in BMI*

	Men	Women	People with diabetes	People without diabetes	Tool used	Source and comments
Change in utility per one unit change in BMI	0.01665	0.0264	0.0285	0.017	TTO	Hakim and colleagues[152] derived utility values from the data on the cohort of 621 patients predominantly female (78%) and white (91%) with the mean age of 42 years and mean BMI of 35 kg/m^2 controlling for age, gender and the health preference value at the beginning of the year
Change in utility per one unit change in BMI			With no diabetes-related complications: 0.01; with diabetes-related complications: 0.016		EQ-5D	Currie and colleagues[178] derived utility values from the hospitalised patients with mean BMI of 29 kg/m^2 controlling for age and peripheral neuropathy
Change in utility per one unit change in BMI	0.0168					Dixon and colleagues[173] derived utility values from 13,152 inpatients and outpatients. Mean BMI was not reported for the entire sample. The results are estimated for patients with BMI > 25 kg/m^2
Change in utility per one unit change in BMI			0.01	0.0079	EQ-5D	Lee and colleagues[179] derived utility values from regression analysis controlling for age but not for gender. The data on inpatients and outpatients included 24,250 people without and 2575 patients with Type 2 diabetes with mean age of 59 and 68 in patients without and with Type 2 diabetes, respectively. The patients were predominantly white (>95%) with mean BMI of 26 kg/m^2 and 29 kg/m^2 in patients without and with Type 2 diabetes, respectively.

BMI, body mass index; EQ-5D, EuroQoL-five dimensions generic, preference-based instrument; TTO, time trade-off technique.

breakdown of open and laparoscopic procedures as in the previous review (see *Table 62*).

The resource use estimates differ from those adopted for the previous review.[15] Duration of surgery and length of stay for laparoscopic gastric bypass and laparoscopic gastric banding are lower than the previous values [235 minutes and six days for laparoscopic gastric bypass (operating time and total length of stay, respectively) and 150 minutes and six days for laparoscopic adjustable gastric banding]. The costings adopted here assume a lower use of high-dependency care following surgery. In the previous review all patients were assumed to spend one day in either HDU or ITU, whereas clinical advice for this update suggested

that patients undergoing laparoscopic procedures typically recover on the ward unless they experience perioperative complications requiring admission to ITU. Patients undergoing open operations are estimated to spend one day in HDU following surgery.

In contrast to the costings developed for the previous review, gastric bypass is estimated to cost more than adjustable gastric banding. The previously estimated values for gastric bypass were £3286 and £3174 for laparoscopic and open procedures, respectively (using values for the 1999/2000 financial year). The equivalent values for adjustable gastric banding were £3751 and £3645.

TABLE 61 *Resource use and cost estimates for bariatric surgery*

Resource use	Unit cost	Open	Laparoscopic
Gastric bypass			
Time in theatre (minutes)	£16 per minute	180	180
Surgeons operating time (per hour)	Consultant: £87.11	2	2
Anaesthetists time (per hour)	Consultant: £72.64	3	3
High cost consumables	£2040 per procedure	1	1
Days on ward	£261 per day	5	5
Days in ITU	£1986 per day	21.1%	7.5%
Days in HDU	£497 per day	78.9%	0
Specialist dietitian	£32 per hour	2	2
Physiotherapy	£38 per hour	1	1
Total cost gastric bypass		£7705	£7042
Adjustable gastric banding			
Time in theatre (minutes)	£16 per minute	120	120
Surgeons operating time (per hour)	Consultant: £87.11	1	1
Anaesthetists time (per hour)	Consultant: £72.64	2	2
High cost consumables	£1440 per procedure	1	1
Days on ward	£261 per day	5	2
Days in ITU	£1986 per day	0	0
Days in HDU	£497 per day	100%	0
Specialist dietitian	£32 per hour	2	2
Physiotherapy	£38 per hour	1	1
Total cost adjustable gastric banding		£5584	£4304

HDU, high-dependency unit; ITU, intensive-care unit.
Anaesthetist's time is assumed to reflect 30 minutes preparation before surgery and 30 minutes recovery following surgery.
It is assumed that two consultant surgeon operators are present for each laparoscopic procedure.
High-cost consumables for gastric bypass are: staples (£1500) and other single-use items (£200). High-cost consumables for adjustable gastric banding are: gastric bands (£1000) and other single-use items (£200). A trust overhead of 20% has been applied to the total high-cost items for both gastric bypass and adjustable gastric banding.

Unit costs applied to the resource use estimates were provided by the finance department at Southampton University Hospital Trust. The ITU, HDU and ward unit costs are based on 2006/7 Reference Costs uprated to 2007/8 values. Ward unit costs are based on the excess cost per bed day for general surgery. Staff costs are based on a consultant anaesthetist with discretionary points, consultant surgeon with discretionary points (MC10) and a specialist registrar (MN25). There is a large difference in the unit cost for theatre time in this review (£960 per hour) compared with the previous review[15] which estimated theatre time at £335 per hour (approximately £470 per hour at 2007/8 prices, uprated using the Hospital and Community Health Services Pay and Prices Index[177]). Specialist dietitian and hospital physiotherapist unit costs were taken from the Unit costs of Health and Social Care.[177]

The included clinical trials provide little additional information on conversion from laparoscopic to open surgery. Moreover it is difficult to generalise the results from clinical trials, which are likely to be undertaken in more specialist centres, with more experience which may be less likely to convert to open procedures than would be the case in other centres. The proportion of cases converting to open procedures is 0%[108] to 23%[131] for laparoscopic Roux-en-Y gastric bypass. For laparoscopic adjustable gastric banding the range in trials reporting conversions is narrower: 0%[110] to 4%.[127]

TABLE 62 *Additional assumptions*

	Gastric bypass	Adjustable gastric banding
Proportion open procedures	10%	8%

Given the limited additional data on the rate of conversion from laparoscopic to open procedures reported in the included trials, we used the values adopted in the previous review, see *Table 62*.

Resource use assumptions for costing non-surgical management of morbidly obese patients have been taken from the previous review,[15] see *Table 63*. Unit costs have been updated using *Unit Costs of Health and Social Care*.[177]

Resource use assumptions for moderately obese patients undergoing the non-surgical weight reduction programme were based on the description of the programme in the clinical trial report by O'Brien and colleagues.[115] The programme consisted of an intensive six-month period of VLCD and pharmacotherapy as well as specialist dietary advice. The resource use assumptions extracted from the clinical trial report and the unit costs applied to the resource estimates are reported in *Table 64*.

The frequency of patients attendance for hospital or primary care, associated with each intervention, was based on estimates developed for the previous review,[15] published literature, discussion with surgical specialists and a costing developed for Aberdeen specialist obesity services (U. Kulkarni, NHS Grampian, 2008, personal communication). All new patients are evaluated in the outpatient department and receive an electrocardiogram. In the previous review the preoperative assessment

schedule assumed that, for every patient undergoing surgery, four patients are screened for eligibility and two undergo workup (by VLCD) to assess suitability for treatment, based on figures reported in Andersen and colleagues.[180] This corresponded to seven outpatient visits, four dietitian consultations and one session with a psychologist. The unit costs and estimated cost per patient undergoing surgery are listed in *Table 65*.

Based on the costing developed in Aberdeen, it was assumed that patients undergoing adjustable gastric banding would make four additional attendances for the initial fill and band adjustments and that they would have additional specialist dietitian consultations associated with these band adjustments. These additional attendances add £428 to the costs of follow-up for patients undergoing adjustable gastric banding.

The costs of managing adverse events were taken into account in our analyses by identifying the proportion of patients having major perioperative complications requiring ITU admission, and the proportion of patients having early reoperation (within 30 days) because of failure of the original operation (typically band slippage for patients undergoing adjustable gastric band procedures or bleeding, stenosis or leakage in patients undergoing gastric bypass). Revision surgery was estimated to cost the same as the original surgical procedure. Complications requiring admission to ITU were costed using the estimated length of ITU admission and the per diem cost (£1986) reported in *Table 61*. The costs were applied to the proportion of patients experiencing perioperative complications requiring ITU admission (7.5% of laparoscopic gastric bypass patients[113,124]) and to the proportion of patients requiring surgical revision (2% for laparoscopic adjustable gastric bypass[110] and 13.5% for gastric bypass[107,108]).

TABLE 63 *Resource use and cost estimates for non-surgical management of morbidly obese patients*

Resource use	Unit cost	Contacts per year
General practitioner	£30	4
Community dietitian	£48	2
Practice nurse	£9	2
District nurse	£24	2
Total cost of non-surgical management		£282

Add cost of 12 weeks of very-low-calorie diet, every three years (£201.60, two ready-mixed Slimfast shakes everyday for 12 weeks)

TABLE 64 *Resource use and cost estimates for non-surgical weight loss programme for moderately obese (BMI ≥ 30 and < 35) patients*

Resource category	Phase of programme	Unit cost	Contacts per period
Contact with physician (in out-patients, every two weeks for intensive phase and every six weeks for remainder)	Intensive phase (0 – 6 months)	First visit: £144	1
		Subsequent: £99	13[a]
	Months 7–12	£99	4[b]
	Months 13–24	£99	9[b]
Total cost of medical management for non-surgical weight loss programme			£2718

Resource category	Phase of programme	Unit cost	Resource Use
Intensive management (diet and pharmacotherapy)	Very-low-calorie diet (0–12 weeks)	£1.27	168
		(1 packet optifast)	(2 per day)
	Transition phase (weeks 13–16)	£1.27	28
		(1 packet optifast)	(1 per day)
		£0.40	28
		(120 mg orlistat)	(1 per day)
	Pharmacotherapy only (weeks 17–26)	£0.40	210
		(120 mg orlistat)	(3 per day)
Postintensive management	Months 7–24	£0.40	1057[c]
		(120 mg orlistat)	(3 per day)
Total cost of very-low-calorie diet and pharmacotherapy for non-surgical weight loss programme			£767

Optifast is a liquid, very-low-calorie diet developed by Novartis Medical Nutrition Corporation and is available in the USA, Canada, New Zealand and Australia. This product was used in the trial reported by O'Brien and colleagues,[115] hence the costings developed here are based on the use of this product. The price per packet reported in this table has been derived from the quoted price for USA and converted to UK pounds using currency conversion rates.
a Estimated on the basis that clinical trial report states that patients were seen every two weeks during the intensive phase.
b Estimated on the basis that the clinical trial report states that patients were seen every four to six weeks following the intensive phase. All patients were seen at least every six weeks.
c Estimated as three 120 mg tablets per day for 78 weeks, adjusted for the fact that 25.8% of non-surgical patients could not tolerate orlistat and a further 9.7% chose not to use it.

Patients are likely to undergo a number of additional surgical procedures as a result of undergoing bariatric surgery, even when the original operation was successful. Expert opinion suggested that 5% of patients undergoing laparoscopic gastric bypass would require an additional operation for repair of internal hernia. Additionally, patients undergoing active weight reduction are at risk of developing gallstones, and may require cholecystectomy. It has been suggested that 35–38% of patients with morbid obesity develop gallstones as they lose weight following bariatric surgery[181–183] (which has led some surgeons to advocate performing cholecystectomy during bariatric surgery). Miller and colleagues[184] observed 12 cholecystectomies in 60 placebo-treated patients during two years follow-up in their trial

of prophylaxis against gallstone formation for patients following vertical banded gastroplasty and adjustable gastric banding (patients had a mean preoperative BMI of 44.3 and were 85% female). De Wit and colleagues reported 8% of patients having a cholecystectomy within one year of bariatric surgery.[132] In the model we assume that 20% of morbidly obese patients undergo cholecystectomy within two years of a bariatric procedure (8% in the first year and 12% in the second, reflecting the observation that the peak incidence of symptomatic gallstones is 16 months after surgery).

Health-state costs
The model, as described in the section Model type and rationale for the model structure, this chapter,

TABLE 65 *Preoperative and postoperative resource use and costs*

Category of resource use		Frequency	Unit cost (£)	Total cost
Preoperative assessment		7 outpatient visits	4 × 144; 3 × 99	£1114
		4 dietitian consultations[a]	32 per hour	
		4 dietitian consultations[b]	32 per hour	
		1 session with a psychologist[c]	67 per hour	
Postdischarge	Primary care in month following discharge	6 GP visits	32 per visit	£306
		2 practice nurse visits	9 per visit	
		4 district nurse visits	24 per visit	
Follow-up care	Year 1	4 outpatient visits	99 per visit	£849
		12 community dietitian contacts[d]	48 per hour	
		2 psychology consultations	67 per hour	
	Year 2	4 outpatient visits	99 per visit	£636
		4 community dietitian contacts[d]	48 per hour	
		2 psychology consultations	67 per hour	
	Year 3 and beyond	2 outpatient visits	99 per visit	£318
		2 community dietitian contacts[d]	48 per hour	
		1 psychology consultations	67 per hour	

Unit costs for outpatient visits are taken from 2006/07 NHS Reference Costs.[185] The remaining costs are taken from *Unit costs of Health and Social Care*.[177]
a   Assumed duration 30 minutes
b   Assumed duration 20 minutes
c   Assumed duration two hours
d   Assumed duration 30 minutes. Add £2.60 pr visit for travel.

consists of five health states (excluding death). Costs for the health state labelled 'no comorbidity' in the state transition diagram, *Figure 2*, consists only of ongoing monitoring for postsurgical patients, or routine follow-up for patients receiving non-surgical intervention. No additional, state-specific, costs are applied to this state. The same assumption holds for the 'remission of comorbidity' health state.

Table 66 reports the health-state costs adopted in the model. The Type 2 diabetes cost is based on the CODE-2 UK[160] estimate of health-care resource use and costs applied in the economic model developed for the previous report. The average cost per patient year (£1505) reported for CODE-2 UK, with a cost year of 1998–9, has been inflated to 2007–8 prices using the Hospital and Community Health Services (HCHS) Pay and Prices Index.[177] The breakdown of costs reported for CODE-2 UK was that 36.2% of costs were attributable to hospital admissions and 37.7% to ambulatory care, with the remainder attributable to drug treatment (22.5%) and insulin (3.5%).

Health-state costs for AMI were based on inputs to the Southampton CHD treatment model (K. Cooper, University of Southampton, 2008, personal communication). The acute costs are based on NHS Reference Costs for non-elective inpatient admission with AMI. Costs for the post-MI health state are based on daily dosage and estimated use of a range of drugs (statins, calcium channel blockers, beta blockers, acetylcholinesterase inhibitors and nitrates) combined with unit costs from the *British National Formulary*, as well as health-care utilisation data from the *Health Survey for England*[17] combined appropriate unit costs.[177] All costs were estimated for the 2005–6 financial year and have been inflated to 2007–8 prices using the HCHS Pay and Prices Index.

TABLE 66 *Health-state costs applied in the economic model*

Health state	Acute (£)	Chronic (£)	Source
Diabetes		2197	Williams and colleagues[160]
AMI	1613	565	Southampton CHD treatment model
Stroke	9540[a]	2565	Ward and colleagues[186]

AMI, acute myocardial infarction; CHD, coronary heart disease.
a Applies for year following stroke.

Health-state costs for stroke were based on costs applied in a recent HTA of statins for the prevention of coronary events.[186] These were derived from a published study[187] estimating the economic burden of stroke in the UK. The acute cost of a stroke was estimated using the cost of acute events reported by Youman and colleagues[187] (mild stroke £5099, moderate stroke £4816 and severe stroke £10,555), weighted by the distribution of severity of strokes. The costs reported by Ward and colleagues[186] were for the financial year 2004–5 and have been inflated to 2007–8 prices using the HCHS Pay and Prices Index.

Discounting of future costs and benefits
A discount rate of 3.5% has been applied to future costs and benefits in line with current guidance. Discount rates of 0% and 6% for costs and 0% and 1.5% for outcomes have been applied in the sensitivity analyses.

Presentation of results
We report findings on the cost-effectiveness of interventions based on analysis of a cohort of patients having baseline age, sex and weight characteristics, as discussed earlier. Surgical procedures are compared with appropriate non-surgical comparators.

We report the results of these comparisons in terms of the incremental gain in QALYs and the incremental costs determined in the cohort analysis.

Assessment of uncertainty in the SHTAC analysis (sensitivity analysis)
Parameter uncertainty in the updated model is addressed using probabilistic sensitivity analysis. Probability distributions are assigned to the point estimates used in the base-case analysis. Appendix 20 reports the variables included in the probabilistic sensitivity analyses, the form of distribution used for sampling and the parameters of the distribution.

In the absence of a robust, pooled estimate of treatment effect (with associated estimate of variability) we felt it was inappropriate to undertake probabilistic sensitivity analysis using the original model. In both models deterministic sensitivity analysis is used to address particular areas of uncertainty in the model related to:

- model structure
- methodological assumptions
- parameters around which there is considerable uncertainty or which may be expected, a priori, to have disproportionate impact on study results.

The purpose of this analysis is to identify clearly the impact of this uncertainty and to test the robustness of the cost-effectiveness results to variation in structural assumptions and parameter inputs.

SHTAC cost-effectiveness model – summary of methods
- The model developed for the previous assessment report was assessed against other published models for completeness and relevance, and the conceptual model was extended to include CHD and stroke. The ability to include these additional health states in the economic model depends on the methods adopted to estimate transitions to these states, which are not typically based on weight-related measures (such as BMI), but use blood pressure and lipid measurements. Where such measurements are reported, the expanded version of the model may be relevant. We propose using the FHS equations to model cardiovascular risks for the expanded model, which require values for blood pressure (systolic or diastolic) and the TC : HDL ratio as well as patients' age, sex, smoking status and whether they have developed diabetes. However, not all studies will report changes in blood pressure and lipid measurements, hence the expanded model may not be applicable to all studies.

- The analysis was developed for three patient populations covered by studies included in the clinical effectiveness review:
  - patients with morbid (Class III, BMI ≥40) obesity undergoing adjustable gastric banding or gastric bypass – as in the previous review
  - patients with severe (Class II, BMI ≥30 and < 40) obesity with significant comorbidity at baseline (Type 2 diabetes) undergoing adjustable gastric banding, based on data from a single trial[117]
  - patients with moderate (Class I, BMI ≥30 and < 35) obesity undergoing adjustable gastric banding, based on data from a single trial.[115]
- The clinical effectiveness review concluded that meta-analysis was not appropriate, hence the model for patients with morbid obesity is not based on robust data synthesis of effectiveness – there was no statistically pooled estimate of each surgical procedure on weight loss and no robust estimate of variability. As a result, the economic model adopted two estimates of the effect of gastric bypass and adjustable gastric banding on weight loss – these were identified as 'optimistic' estimates (based on the previous assessment report) and an alternative 'pessimistic' estimate (based on a recently published trial comparing gastric bypass and adjustable gastric banding). Outcomes, in terms of weight loss at five years following surgery, were extrapolated using data from the SOS study.[97]
- Included trials for patients with morbid obesity did not report change in both blood pressure and suitable lipid measurements – hence the model developed for the previous assessment report has been used for this population, with updated assumptions on costs, diabetes incidence, permanency of diabetes remission following surgery and on the impact of BMI on health-state utility.
- The clinical trials reporting the use of adjustable gastric banding for severely obese (BMI ≥30 and < 40) patients with Type 2 diabetes and for moderately obese (BMI ≥30 and < 35) patients reported sufficient information, up to two years of follow-up, to apply the new model. The analysis for these patients will initially be undertaken for the period of the trial follow-up only, and will then use extrapolations based on data from the SOS study, where relevant, or on the basis of data reported in the trial.

- In the absence of a robust, pooled estimate of treatment effect (with associated estimate of variability) we felt it was inappropriate to undertake probabilistic sensitivity analysis using the original model. The robustness of the model results to variation in assumptions and parameter values was assessed using deterministic sensitivity analysis. Probabilistic sensitivity analysis would be used for the updated model, but would primarily address uncertainty in parameter values – uncertainty over model structure and methods for extrapolating trial results would be addressed using deterministic sensitivity analysis.

Results

The first of the next eight section reports results for the base-case analysis of adjustable gastric banding and gastric bypass compared with non-surgical management for patients with morbid obesity (BMI ≥40), using baseline characteristics described in the section Baseline cohort of patients with morbid obesity, this chapter. Total costs for all management strategies are reported, as are the total QALYs under the optimistic and pessimistic assumptions regarding weight loss. ICERs are reported for both surgical procedures relative to non-surgical management. The principal differences between the results of this analysis and the previous assessment report are identified and explanations provided. The deterministic sensitivity analysis of adjustable gastric banding and gastric bypass compared with non-surgical management for patients with morbid obesity is then discussed. In the absence of a robust, pooled estimate of treatment effect (with associated estimate of variability) we felt it was inappropriate to undertake probabilistic sensitivity analysis using the original model.

The third section reports on results for the base-case analysis of adjustable gastric banding compared with non-surgical management for patients with moderate-to-severe obesity (BMI ≥30 and < 40) and Type 2 diabetes, based on the trial reported by Dixon and colleagues.[117] The following two sections report the deterministic sensitivity analysis and a probabilistic sensitivity analysis of adjustable gastric banding compared with non-surgical management for patients with moderate-to-severe obesity (BMI ≥30 and < 40) and Type 2 diabetes. The probabilistic sensitivity analysis primarily addresses uncertainty in parameter values – uncertainty over model structure and

methods for extrapolating trial results is addressed using deterministic sensitivity analysis.

Results for the base-case analysis of adjustable gastric banding compared with an intensive management programme for patients with moderate obesity (BMI ≥30 and <35) are reported, based on the trial reported by O'Brien and colleagues.[115] Finally, the deterministic sensitivity analysis and a probabilistic sensitivity analysis are reported. As stated above, the probabilistic sensitivity analysis primarily addresses uncertainty in parameter values–uncertainty over model structure and methods for extrapolating trial results is addressed using deterministic sensitivity analysis.

Cost-effectiveness of bariatric surgery (gastric bypass or adjustable gastric banding) for morbid obesity (BMI ≥40)–base-case analysis

Table 67 reports the total costs and total QALYs for the baseline cohort of morbidly obese patients undergoing gastric bypass, adjustable gastric banding and non-surgical management, using the updated assumptions with regard to surgery cost, efficacy (in terms of weight reduction, impact on diabetes incidence and on remission of Type 2 diabetes) and health-state utility. The model has been estimated over a 20-year time horizon, as in the previous assessment report. All costs and outcomes are discounted at 3.5%.

Surgical management of obesity is estimated to be more costly than non-surgical management, but results in improved outcomes (in terms of QALYs) over the modelled 20-year time horizon. Two scenarios are modelled that effect outcomes, but not cost. Assumptions on weight loss, up to five years, adopted in the previous assessment report have been extrapolated to 10 years using data for gastric bypass and gastric banding from the SOS

study.[97] An alternative scenario was constructed using data, with five years follow-up, from the trial reported by Angrisani and colleagues[107] with a similar extrapolation to 10 years using data from the SOS study.[97] This gave generally less favourable estimates in terms of weight loss, particularly for gastric banding.

Compared with the previous assessment report, total QALYs associated with non-surgical management are lower, while the total QALYs for surgical management are higher. This is the result of changes in discounting practice, updated assumptions on duration of weight reduction and alternative assumptions regarding the health gain associated with weight loss. The effect of change in discounting practice, alone, would be to reduce the QALYs associated with each treatment strategy by approximately 1.7 QALYs. Extrapolating weight loss assumptions up to 10 years, alone, increases the total QALYs associated with surgical intervention by approximately 4% (with no impact on outcomes for non-surgical management because the baseline assumption is that patients receiving non-surgical management neither gain nor lose weight). Updated assumptions on the utility gain associated with weight loss increases the total QALYs associated with non-surgical management by approximately 13% and increases the total QALYs associated with surgical management by approximately 18%.

Total costs of non-surgical management and gastric bypass are approximately double the estimates included in the previous assessment report, while costs for adjustable gastric banding are approximately 60% higher. The increase in total costs is the result of a combination of changes in discounting practice, updated assumptions regarding incidence and remission of Type 2 diabetes in patients undergoing surgery and receiving non-surgical management and updated

TABLE 67 *Total discounted costs and total discounted QALYs for surgical and non-surgical management of morbid obesity (BMI ≥40), using updated assumptions, based on weight reduction adopted for previous assessment report[188] and based on weight reduction reported by Angrisani and colleagues[107]*

Treatment	Total cost (£)	QALYs[a]	QALYs[b]
Non-surgical management	13,561	10.80	10.80
Adjustable gastric banding	17,126	12.68	11.72
Gastric bypass	19,824	12.78	12.32

QALYs, quality-adjusted life-years.
a 'optimistic'–based on weight reduction estimates developed for previous assessment report.[188]
b 'pessimistic'–based on weight reduction reported by Angrisani and colleagues.[107]

costing assumptions. For non-surgical management 36% of the difference can be attributed to changes in discounting practice alone and 44% to changes in costs alone, whereas for gastric bypass 22% of the difference can be attributed to changes in discounting practice and 73% to changes in costing assumptions. Aside from the general increase in the estimated total costs for each strategy, the other main difference from the previous assessment report is that total costs for gastric bypass are approximately £2600 higher than for adjustable gastric banding, whereas total costs for adjustable gastric banding were approximately £1000 higher than for gastric bypass in the previous report. This is primarily the result of the shorter duration of surgery for adjustable gastric banding (60 minutes versus 120 minutes for laparoscopic gastric bypass) and shorter LOS (two days for adjustable gastric banding versus five days for gastric bypass).

Table 68 reports the incremental cost-effectiveness of gastric bypass and adjustable gastric banding each compared with non-surgical management.

Surgical management of morbid obesity, using adjustable gastric banding or gastric bypass provides additional QALYs at additional cost under both scenarios – extrapolating weight reduction to 10 years based on data from the previous assessment report[188] and the trial reported by Angrisani and colleagues.[1107] The ICERs range between £1897 and £4127 per QALY gained, which are within the range conventionally deemed as cost-effective from an NHS decision-making perspective.

The incremental cost for gastric bypass is around 60% greater than for adjustable gastric banding, which contrasts with the previous assessment report, where gastric bypass was less costly than adjustable gastric banding. This is largely the result

of changes in assumptions over duration of surgery, which have affected adjustable gastric banding disproportionately (duration of laparoscopic adjustable gastric banding was assumed to be 60 minutes, in contrast with 150 minutes in the previous report, whereas duration of laparoscopic gastric bypass was assumed to be 120 minutes, in contrast with 235 minutes in the previous report) and length of stay (length of stay for laparoscopic adjustable gastric banding was assumed to be two days, in contrast with five days in the previous report, whereas length of stay for laparoscopic gastric bypass was assumed to be five days, in contrast with six days in the previous report).

The QALY gain associated with surgical management of morbid obesity is approximately two, when based on assumptions on weight reduction adopted in the previous report and between 1 and 1.5 when based on the results of the trial reported by Angrisani and colleagues. These QALY gains are larger than those estimated in the previous report (0.45 QALYs when compared with non-surgical management). These differences are primarily the result of extrapolating the weight reduction assumptions up to 10 years (resulting in an approximate doubling of the QALY gain) and updated assumptions on the utility gain associated with reduction in BMI. The impact of alternative assumptions on the utility gain associated with reduction in BMI is explored in a deterministic sensitivity analysis.

Cost-effectiveness of bariatric surgery (gastric bypass or adjustable gastric banding) for morbid obesity (BMI ≥ 40) – deterministic sensitivity analysis

A series of one-way sensitivity analyses were conducted using the updated model. These are reported in *Table 69*, which also includes results for some scenario analyses presented in the previous

TABLE 68 Incremental cost-effectiveness of gastric bypass and adjustable gastric banding compared with non-surgical management

| Intervention | Incremental cost (£) | 'Optimistic' weight reduction from previous assessment report[188] | | 'Pessimistic' weight reduction from Angrisani and colleagues[107] | |
		Incremental QALYs	ICER (£)	Incremental QALYs	ICER (£)
AGB	3566	1.88	1897	0.92	3863
GBP	6263	1.98	3160	1.52	4127

AGB, adjustable gastric banding; GBP, gastric bypass, ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life-years.
Incremental cost and incremental QALYs for both AGB (adjustable gastric banding) and GBP (gastric bypass) are estimated relative to non-surgical management.

assessment report (for example, Scenario five from the previous report which examined the impact of involving surgeons with less experience of bariatric surgery on the cost-effectiveness of surgical management of morbid obesity – see rows titled 'Surgeon experience' in *Table 69*). Other scenarios considered in the sensitivity analysis include:

- altering assumptions for operative mortality from 1% to 0.5% for gastric bypass and from 0% to 0.05% for adjustable gastric banding
- reducing the change in utility associated with a unit change in BMI (from 0.0166 to 0.0075)
- applying BMI-specific incidence of Type 2 diabetes, rather than values for the surgical (all surgery, not specific to gastric bypass or adjustable gastric banding) and non-surgical cohorts from the SOS study[97]
- allowing band adjustments in the second and/ or third year rather than four only in year one
- considering the impact of surgeon inexperience – on duration of surgery, on revision rates and on outcome (in terms of weight reduction)
- increasing elements of surgical cost by 20%
- varying costs of health-service contacts for patients on the intensive programme
- consider the cost impact of a higher rate of abdominoplasty following surgically-induced weight loss and including cost impact of complications of abdominoplasty.

In general the results are robust to changes in assumptions, reported in *Table 69*, and in all cases the ICERs remain within the range conventionally deemed as cost-effective from an NHS decision-making perspective. However, changes in some key assumptions produce less favourable cost-effectiveness estimates than the base case adopted for this analysis:

- Adopting a lower utility gain for reductions in BMI has a large impact on the QALY gain associated with surgical management; reducing from 1.88 to 0.85 for adjustable gastric banding and from 1.98 to 0.85 for gastric bypass, for the optimistic assumption on weight reduction, when the utility gain per unit BMI reduction is reduced from 0.017 to 0.0075. Equivalent values using pessimistic assumptions are a reduction from 0.92 to 0.42 and from 1.52 to 0.64 for adjustable gastric banding and gastric bypass respectively.
- Using BMI-specific incidence of Type 2 diabetes has a greater impact on incremental costs for adjustable gastric banding when using

weight reduction from the trial reported by Angrisani and colleagues[107] than is the case for gastric bypass (or for either approach to surgical management when using assumptions for weight reduction adopted in the previous assessment report). The effect of using BMI-specific diabetes incidence is to increase incremental costs for adjustable gastric banding by approximately £1750 so that the ICER rises from £3863 to £5749.

- Increasing operative costs by 20% increases incremental costs for adjustable gastric banding by approximately £1000 and gastric bypass by approximately £1500. This increases the ICER for adjustable gastric banding from £1897 to £2416 using assumptions for weight reduction adopted in the previous assessment report, and from £3863 to £4921 based on the trial results reported by Angrisani and colleagues.[107] The equivalent changes for gastric bypass are from £3160 to £3963, and from £4127 to £5176.
- Increasing postoperative costs by 20% increases incremental costs by between £1200 and £1300. This increases the ICER for adjustable gastric banding to £2579 using assumptions for weight reduction adopted in the previous assessment report, and to £5252 based on the trial results reported by Angrisani and colleagues.[107] The equivalent changes for gastric bypass are an increase to £3758, and to £4908.
- Increasing all surgery-related costs by 20% leads to a higher proportionate increase for adjustable gastric banding, with incremental costs increasing by approximately £2500 (70% increase). The equivalent value for gastric bypass is approximately £3000 (48% increase). The ICER for adjustable gastric banding increases to £3217 using assumptions for weight reduction adopted in the previous assessment report, and to £6551 based on the trial results reported by Angrisani and colleagues.[107] The equivalent changes for gastric bypass are an increase to £4674, and to £6103.
- Repeating the scenario analysis, presented in the previous assessment report, for surgical experience leads to increased costs (because of increased duration in surgery and increases in the rate of revision) and poorer outcomes (i.e. reduced QALYs because of increased operative mortality and lower weight reduction). The effect of these altered assumptions is shown cumulatively, with the effects on costs considered first. Increasing duration of surgery and revision rates leads to similar proportionate increases in incremental

TABLE 69 *Deterministic sensitivity analysis for cost-effectiveness of surgical management (gastric bypass or adjustable gastric banding) of morbid obesity (BMI ≥ 40)*

		Incremental cost (£)	'Optimistic' weight reduction from previous assessment report[188]		'Pessimistic' weight reduction from Angrisani and colleagues[107]	
			Incremental QALYs	ICER (£)	Incremental QALYs	ICER (£)
Base case	AGB	3566	1.88	1897	0.92	3863
	GBP	6263	1.98	3160	1.52	4127
Operative mortality	AGB	3559	1.87	1906	0.91	3905
(AGB = 0.05%; GBP = 0.5%)	GBP	6293	2.05	3075	1.58	3983
Health-state utility	AGB	3566	0.85	4215	0.42	8584
(0.0075 gain per unit BMI reduction)	GBP	6263	0.85	7412	0.64	9845
Use BMI-specific incidence of Type 2 diabetes (see *Table 59*)	AGB	3873	1.88	2060		
	GBP	6297	1.98	3177		
	AGB	5307			0.92	5749
	GBP	6814			1.52	4490
Increase cost of preoperative assessment by 20%	AGB	3788	1.88	2015	0.92	4104
	GBP	6486	1.98	3272	1.52	4273
Increase operative costs by 20%	AGB	4542	1.88	2416	0.92	4921
	GBP	7855	1.98	3963	1.52	5176
Increase postoperative costs by 20%	AGB	4848	1.88	2579	0.92	5252
	GBP	7448	1.98	3758	1.52	4908
Increase all costs by 20%	AGB	6048	1.88	3217	0.92	6551
	GBP	9262	1.98	4674	1.52	6103
Band adjustments in second year (four)	AGB	3965	1.88	2109	0.92	4295
	GBP	6263	1.98	3160	1.52	4127
Band adjustments in second year (four) and third year (two)	AGB	4152	1.88	2208	0.92	4497
	GBP	6263	1.98	3160	1.52	4127
Late reoperations for AGB continue over 10 years (6%)	AGB	5240	1.88	2787	0.92	5676
	GBP	6263	1.98	3160	1.52	4127
Late reoperations for AGB continue over 10 years (2.5%)	AGB	3957	1.88	2105	0.92	4286
	GBP	6263	1.98	3160	1.52	4127
Surgeon experience: increase duration of surgery (50%) and double revision rates	AGB	5685	1.88	3024	0.92	6159
	GBP	9588	1.98	4838	1.52	6318
Surgeon experience: double operative mortality; (GBP = 2% AGB = 0%)	AGB	5685	1.88	3024	0.92	6159
	GBP	9528	1.85	5143	1.39	6839
Surgeon experience: reduce estimated weight loss by 25%	AGB	5685	1.41	4019	0.70	8091
	GBP	9528	1.34	7135	0.99	9631
Cost cholecystectomy as a day case	AGB	3445	1.88	1833	0.92	3732
	GBP	6143	1.98	3099	1.52	4048
Cost abdominal hernia procedures as day case	AGB	3566	1.88	1897	0.92	3863
	GBP	6205	1.98	3131	1.52	4088

TABLE 69 *Deterministic sensitivity analysis for cost-effectiveness of surgical management (gastric bypass or adjustable gastric banding) of morbid obesity (BMI ≥ 40) (continued)*

		Incremental cost (£)	'Optimistic' weight reduction from previous assessment report[188]		'Pessimistic' weight reduction from Angrisani and colleagues[107]	
			Incremental QALYs	ICER (£)	Incremental QALYs	ICER (£)
Adjust abdominoplasty cost for complications (25% with intermediate complication and 5% with major complication)	AGB	3589	1.88	1909	0.92	3888
	GBP	6286	1.98	3172	1.52	4142
Higher rate of apronectomy	AGB	3901	1.88	2075	0.92	4226
	GBP	6599	1.98	3330	1.52	4348
Patients recover in HDU (1 day) rather than on ward	AGB	3766	1.88	2003	0.92	4079
	GBP	6426	1.98	3243	1.52	4234
Include conversion to open procedures	AGB	3677	1.88	1956	0.92	3983
	GBP	6329	1.98	3194	1.52	4170

AGB, adjustable gastric banding; BMI, body mass index; GBP, gastric bypass; HDU, high-dependency unit; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life-years.

costs [increase of approximately £2200 (59% increase) for adjustable gastric banding and £3325 (54% increase) for gastric bypass]. The ICER for adjustable gastric banding increases to £3024 using assumptions for weight reduction adopted in the previous assessment report, and to £6159 based on the trial results reported by Angrisani and colleagues.[107] The equivalent changes for gastric bypass are an increase to £4838, and to £6318. Doubling operative mortality has no effect on adjustable gastric banding (because operative mortality was assumed to be zero), but reduces the QALY gain for gastric bypass to 1.85 using weight loss assumptions from the previous report and 1.39 using assumptions based on Angrisani and colleagues.[107] Reducing estimated weight loss by 25% reduces the QALY for surgical management by around 0.5 QALYs (using weight loss assumptions from the previous report) resulting in an ICER of £4019 for adjustable gastric banding and £7135 for gastric bypass. The equivalent values using assumptions based on Angrisani and colleagues are £8091 for adjustable gastric banding and £9631 for gastric bypass.

Cost-effectiveness of bariatric surgery (adjustable gastric banding) for moderate to severe obesity (BMI ≥ 30 and < 40), with Type 2 diabetes – base-case analysis
Table 70 reports the total costs and total QALYs for the baseline cohort of moderately-to-severely

obese patients (BMI ≥ 30 and < 40) undergoing adjustable gastric banding and non-surgical management – see section on Baseline cohort of patients, this chapter, with morbid obesity for the assumptions made for this cohort. All costs and outcomes are discounted at 3.5%.

The estimated cost of surgery is based on the assumptions outlined in *Table 61*, with regard to operating time, length of stay and costs of consumables. Costs associated with reoperations as the result of failure of the initial surgery or reoperation because of late complications were based on complication rates reported for the trial population (3.3% reoperations caused by initial failures and 6.7% reoperation for late complications).[117] Costs for the conventional-therapy programme were based on the trial report, which stated that patients met with a member of the team (general physician, dietitian, nurse or diabetes educator) every six weeks throughout the two years of the trial. It was assumed, as with the postdischarge routine for surgical patients, that non-surgical patients would have more frequent consultations with dietitians than with general medical support – hence it was assumed that the conventional therapy programme consisted of six additional consultations with a dietitian and three additional outpatient visits. The components of the programme that were related to patients' diabetes care was assumed to be included in the health-state costs for diabetes.

TABLE 70 *Total discounted and incremental costs, total discounted and incremental QALYs and ICERs for surgical (adjustable gastric banding) and non-surgical management of moderate-to-severe obesity (BMI ≥ 30 and < 40), with Type 2 diabetes, adopting varying model time horizons*

	Model time horizon								
	2 years			5 years			20 years		
	Non-surgical	Surgical	Difference	Non-surgical	Surgical	Difference	Non-surgical	Surgical	Difference
Cost (£)	4842	9874	5032	10,628	13,425	2796	31,683	33,182	1500
QALYs	1.47	1.74	0.27	3.48	4.09	0.61	10.39	11.49	1.10
ICER (£)			18,930			4580			1367

ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life-years.

Table 70 reports results for three time horizons:

- two years, which corresponds to the duration of the clinical trial report[117]
- five years, where outcomes reported in the clinical trial have been extrapolated beyond two years, based on data on trends in weight reduction over time reported for the gastric banding cohort in the SOS study[97] and on reported durability of diabetes remission reported for all surgically managed patients in the SOS study (discussed in the Effectiveness – diabetes resolution section, this chapter)
- twenty years, where outcomes reported in the clinical trial have been extrapolated up to 10 years following surgery using trends reported for the SOS study,[97] as discussed above. At 10 years following surgery it is assumed that weight, blood pressure and lipid measurements return to their baseline levels. It is also assumed that all patients who previously resolved Type 2 diabetes, either following surgery or through conventional treatment, and remained in the postdiabetic state up to 10 years would then relapse and return to the diabetic health state.

Surgical management of moderate-to-severe obesity (BMI ≥30 and < 40) in patients with Type 2 diabetes is estimated to be more costly, but also results in improved outcomes (in terms of QALYs) over each of the modelled time horizons. Costs for the surgical cohort are approximately double the costs for the non-surgical cohort, when adopting a two-year time horizon. However, as the time horizon increases, the proportionate difference and the absolute difference in costs between the surgical and non-surgical cohorts decreases. This is largely because of the dominant effect of diabetes-related costs for the non-surgical cohort, where only 13% of the cohort achieve remission of Type 2 diabetes

in contrast with 73% of the surgically-treated cohort, and where 83% of total costs are associated with the diabetes health state cost. As a result of this, total costs for the non-surgical cohort increase by over 100% moving from the two-year to the five-year time horizon, whereas the increase is around 36% for the surgical cohort. The proportionate increase, when moving from the five-year to the 20-year time horizon, is more similar between the two cohorts, because differences in diabetes resolution and weight loss are only extrapolated up to 10 years in the model – at that point patients in both cohorts are assumed to revert to baseline values.

The total discounted QALYs with surgical management are greater than with non-surgical management for each of the time horizons modelled, with the incremental gain increasing with increasing time horizon. The proportionate increase, for surgical over non-surgical management, is approximately the same for a two-year and five-year time horizon (18.4% at two years and 17.5% at five years), but drops slightly for the 20-year time horizon (10.6%). As with the costs, this reflects the fact that trial outcomes are extrapolated up to 10 years, with both cohorts reverting to baseline values at that point.

Cost-effectiveness of bariatric surgery (adjustable gastric banding) for moderate to severe obesity (BMI ≥30 and < 40), with Type 2 diabetes – deterministic sensitivity analysis

A series of one-way sensitivity analyses were conducted for each time horizon. These are reported in *Table 71*. In all cases the least favourable ICERs are associated with the short model time horizon, ranging from around £19,000 per QALY gained up to £35,000 per QALY gained. More favourable ICERs are found for the five-year and 20-year time horizons, ranging from around

£1300 per QALY gained up to £10,000 per QALY gained. In all scenarios, for longer time horizons, the ICERs remain within the range conventionally deemed as cost-effective from an NHS decision-making perspective.

In general the sensitivity analyses are similar to those described in the previous section. However, some entries in *Table 71* may require further explanation. The first entry in the table, labelled 'Gradual decline in weight', tests the influence of the assumption that the weight reduction reported at two years following surgery occurs immediately following surgery. This assumption may not be realistic, given the data reported in *Table 52* for percentage weight reduction following gastric banding over time (in trials of patients with morbid obesity) or the data reported in *Table 55* (percentage weight reduction following gastric banding over time in patients with moderate obesity) which show a gradual decline over the first year following surgery. To estimate this gradual decline, the proportion of total weight loss at six-month intervals (up to two years) was estimated from the trial reported by O'Brien and colleagues.[115] These proportions were then applied to the total weight loss observed at two years in the trial reported by Dixon and colleagues,[117] where patients with moderate obesity lost 21.6% of their baseline weight by two years. The proportion of total weight loss at six-month periods reported by O'Brien and colleagues[115] was 65% at six months, 91% at 12 months, 97% at 18 months and 100% at 24 months. The two different assumptions on percentage of weight lost are illustrated in *Figure 4*.

Other scenarios considered in the sensitivity analysis include:

- reducing the change in utility associated with a unit change in BMI (from 0.0166 to 0.0075)
- including a low operative mortality for surgery (0.05% rather than zero in the base case)
- allowing band adjustments in the second and/or third year rather than four only in year one
- considering the impact of surgeon inexperience – on duration of surgery, on revision rates and on outcome (in terms of weight reduction).

In general the results are robust to changes in assumptions. However, changes in some key assumptions produce less favourable cost-effectiveness estimates than the base case adopted for this analysis.

- Assuming a gradual decline in weight, rather than applying the reduction observed at two years immediately following surgery, has a large impact on the ICER at two years (by reducing the QALY gain with surgery by around 20%). However, the effect of this changed assumption is greatly reduced when longer time horizons are considered;
- Applying a lower utility gain for reduction in BMI has a large impact on the QALY gain associated with surgery, reducing from 0.27 to 0.14 at two years (applying a utility gain per unit BMI reduction of 0.0075, the value adopted in the previous review). This effect is maintained over the varying time horizons of
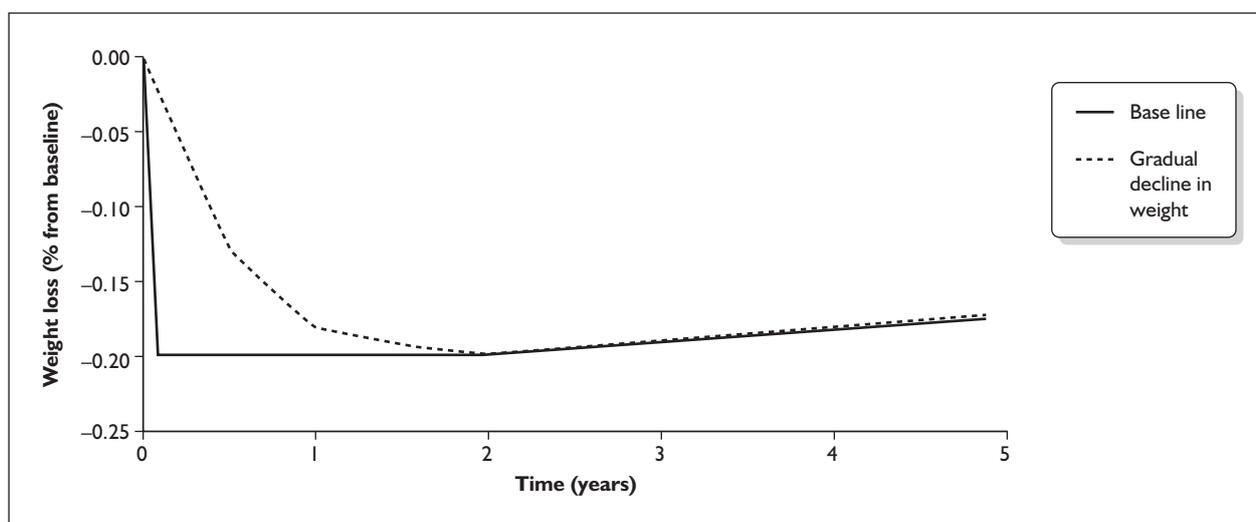
FIGURE 4 *Base-case assumption on weight reduction contrasted with gradual decline in weight for moderate to severely obese patients (BMI ≥ 30 and < 40), with Type 2 diabetes undergoing adjustable gastric banding.*

TABLE 71 Deterministic sensitivity analysis for cost-effectiveness of surgical management (adjustable gastric banding) of moderate-to-severe obesity (BMI ≥30 and <40), with Type 2 diabetes

| | Model time horizon | | | | | | | | |
| | 2 years | | | 5 years | | | 20 years | | |
	Incr. cost (£)	Incr. QALYs	ICER (£)	Incr. cost (£)	Incr. QALYs	ICER (£)	Incr. cost (£)	Incr. QALYs	ICER (£)
Base case	5032	0.27	18,930	2796	0.61	4580	1500	1.10	1367
Gradual decline in weight (base on proportions at six-month intervals in trial reported by O'Brien and colleagues[115]	5032	0.21	23,746	2796	0.56	5024	1500	1.04	1438
Health-state utility (0.0075 gain per unit reduction in BMI)	5032	0.14	34,990	2796	0.33	8538	1500	0.61	2455
Operative mortality (0.1%)	5029	0.26	19,039	2789	0.61	4599	1473	1.09	1357
Operative mortality (0.05%)									
Band adjustments in second year (4)	5446	0.27	20,486	3210	0.61	5257	1913	1.10	1744
Band adjustments third year (2)	5645	0.27	21,237	3409	0.61	5585	2113	1.10	1926
Surgeon experience: increase duration of surgery (50%) and double revision rates	6900	0.27	25,958	4664	0.61	7641	3368	1.10	3070
Surgeon experience: reduce estimated weight loss by 25%	6900	0.21	33,273	4664	0.48	9813	3368	0.87	3866
Increase cost of preoperative assessment by 20%	5255	0.27	19,768	3019	0.61	4945	1723	1.10	1570
Increase operative cost by 20%	5977	0.27	22,484	3741	0.61	6128	2445	1.10	2228
Increase postoperative costs by 20%	5379	0.27	20,235	3314	0.61	5428	2610	1.10	2379
Increase all costs by 20%	6546	0.27	24,627	4481	0.61	7341	3778	1.10	3443
Reduction in SBP (increase by 50% for surgical patients)	5024	0.27	18,897	2790	0.61	4566	1524	1.10	1380
Reduction in TC:HDL ratio (increase by 50% for surgical patients)	5024	0.27	18,887	2793	0.61	4563	1579	1.12	1413
Reduction in SBP and TC:HDL ratio (increase by 50% for surgical patients)	5017	0.27	18,855	2787	0.61	4550	1601	1.12	1424
Reduce diabetes health state cost by 50%	6184	0.27	23,265	5165	0.61	8461	4863	1.10	4432

BMI, body mass index; ICER, incremental cost-effectiveness ratio; Incr. = incremental; QALYs, quality-adjusted life-years; SBP, systolic blood pressure; TC:HDL, total cholesterol to high-density lipoprotein ratio.

the model, with the QALY gain being reduced by between 45% and 48%. The effect of this is to raise the ICER at two years to £35,000 per QALY gained, above a cost-effectiveness threshold considered acceptable from an NHS decision-making perspective.

- Repeating the scenario analysis described earlier for surgical experience leads to increased costs (because of increased duration in surgery and increases in the rate of revision) and poorer outcomes (i.e. reduced QALYs because of lower weight reduction). The effect of these altered assumptions is shown cumulatively, with the effects on costs considered first. Increasing duration of surgery and revision rates leads to an increase in incremental costs of approximately £1900, an increase of 37% at two years and 125% increase at 20 years. The ICER increases to £25,958 at two years and £3070 at 20 years. Reducing estimated weight loss by 25% reduces the QALY for surgical management by around 0.06 QALYs at two years and 0.23 QALYs at 20 years (approximately 22% and 21% reduction, respectively) resulting in an ICER of £33,273 at two years and £3866 at 20 years.

- Increasing operative costs by 20% increases incremental costs for surgery by approximately £950 increasing the ICER at two years to £22,484 (£2228 at 20 years). Increasing postoperative costs by 20% increases incremental costs by approximately £350, increasing the ICER to £20,235 at two years and £2379 at 20 years. Increasing all surgery-related costs by 20% leads to an increase in incremental costs increasing by approximately £1500, increasing the ICER to £24,627 at two years and £3443 at 20 years.

- The impact of decreasing the diabetes health state cost by 50% on incremental costs is larger as the model time horizon increases. The proportionate increase in incremental cost at two years is 23%, whereas at 20 years it is 224%. This arises from the dominant effect of diabetes costs in the non-surgical cohort, in conjunction with the assumption that surgically treated patients who resolve Type 2 diabetes will achieve a maximum remission of 10 years.

Cost-effectiveness of bariatric surgery (adjustable gastric banding) for moderate to severe obesity (BMI ≥ 30 and < 40), with Type 2 diabetes – probabilistic sensitivity analysis

In a probabilistic sensitivity analysis, where percentage weight loss, reduction in systolic

blood pressure and TC:HDL ratio, proportion of patients with remission of Type 2 diabetes (and rate of relapse up to 10 years), health-state utility and health-state costs were sampled probabilistically, all simulations produced incremental cost-effectiveness estimates that were in the north-east quadrant of the cost-effectiveness map when adopting a two-year time horizon (*Figure 5*). That is, all simulations are associated with increased QALYs, but also increased costs. However, when the time horizon was extended to 20 years, while all simulations showed increased QALYs a proportion have negative incremental costs (total discounted costs for the surgical cohort are lower than for the non-surgical cohort). Simulations where costs for the surgically treated cohort are lower than for the non-surgical cohort are most likely to be associated with high proportions of patients with remission of Type 2 diabetes.

In this analysis surgical management with adjustable gastric banding had a probability of being cost-effective (compared with non-surgical management) of 17.5% at a willingness-to-pay threshold of £20,000 per QALY and 83.8% at a willingness-to-pay threshold of £30,000 per QALY for a time horizon of two years when assuming weight loss observed at two years occurs immediately after surgery (*Figure 6*). If the simulations are rerun assuming a gradual reduction in weight following surgery the probability of being cost-effective, with a two-year time horizon falls to 2.5% at a willingness-to-pay threshold of £20,000 per QALY and 50.6% at a willingness-to-pay threshold of £30,000 per QALY. In contrast, for a 20-year time horizon, the probability of surgical management being cost-effective is 100% at both willingness-to-pay thresholds, irrespective of assumptions regarding the pattern of early weight loss (see *Figure 6*).

Cost-effectiveness of bariatric surgery (adjustable gastric banding) for moderate obesity (BMI ≥ 30 and < 35) – base-case analysis

Table 72 reports the total costs and total QALYs for the baseline cohort of moderately obese (BMI ≥ 30 and < 35) patients undergoing adjustable gastric banding and non-surgical management – see section Baseline cohort of patients with morbid obesity, this chapter, for assumptions on this cohort. All costs and outcomes are discounted at 3.5%. The estimated cost of surgery is based on assumptions outlined in *Table 61*, with regard to operating time, length of stay and costs of consumables. Costs associated with reoperations
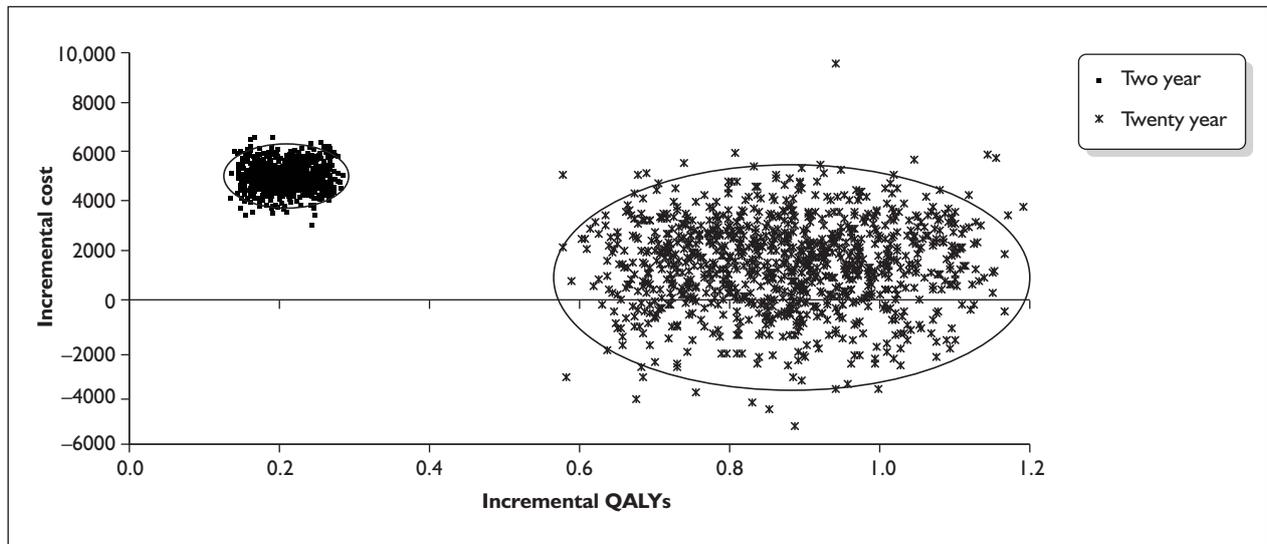
FIGURE 5 *Cost-effectiveness plane – incremental costs and incremental QALYs for patients with moderate to severe obesity (BMI ≥ 30 and < 40), with Type 2 diabetes, undergoing adjustable gastric banding compared with conventional treatment. QALYs, quality-adjusted life-years.*

because of failure of the initial surgery or reoperation as the result of late complications were based on complication rates reported for the trial population [0 reoperations for initial failures and 10% (4/39, three in year 1 and one in year 2) reoperation rate because of late complications in the first and second year following surgery].[115] In addition, one patient had an elective laparoscopic cholecystectomy in the second year following initial surgery.

Costs for the intensive medical programme were based on the trial report,[115] which stated

that patients were seen in outpatient setting by a physician every two weeks for the intensive phase (first six months) of the programme and every six weeks for the remainder of the two-year intervention period. During the intensive phase patients initiated a VLCD for the first 12 weeks, combined VLCD with initiation of pharmacotherapy with orlistat over the next four weeks, before transitioning to pharmacotherapy only (see *Table 64* for costing assumptions). It was reported that eight patients could not tolerate orlistat and three others chose not to use it – the costs of pharmacotherapy in the postintensive
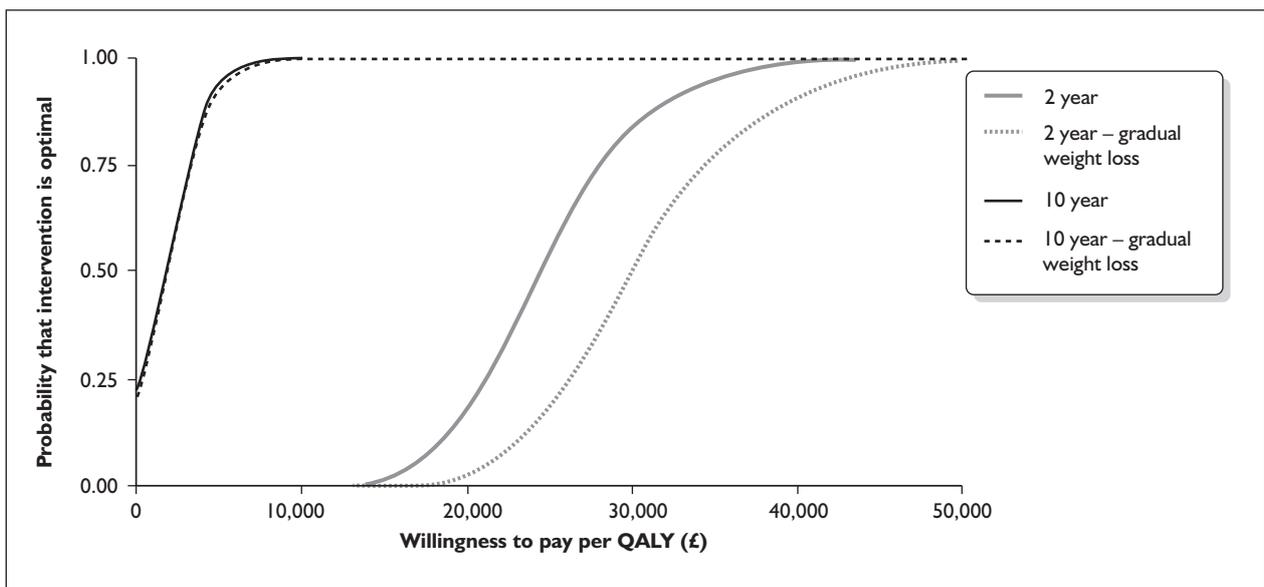
FIGURE 6 *Cost-effectiveness acceptability curves for adjustable gastric banding in patients with moderate to severe obesity (BMI ≥ 30 and < 40), with Type 2 diabetes.*

management phase of the programme have been adjusted to take account of this. The principal cost relating to adverse events in the non-surgical cohort relate to surgical procedures related to cholecystitis. The trial report stated that four non-surgical patients developed acute cholecystitis and underwent elective laparoscopic cholecystectomy (three in year one, and one in year two, corresponding to surgical rates of 10% and 3.7% respectively). It was assumed that non-surgical patients reverted to standard non-surgical management (see *Table 63*) after two years on the weight loss programme.

Table 72 reports results for three time horizons:

- two years, which corresponds to the duration of clinical trial report[115]
- five years, where outcomes reported in the clinical trial have been extrapolated beyond two years, based on data on the trend in weight reduction observed in the non-surgical cohort, where BMI was tending to revert to the baseline value (see *Figure 3*)
- 20 years, where outcomes reported in the clinical trial have been extrapolated using methods discussed above. By the 20-year time horizon all patients are assumed to have reverted to baseline weight and those patients who achieved remission of Type 2 diabetes will have relapsed.

Surgical management of moderately obese patients with adjustable gastric banding is estimated to be more costly, but also results in improved outcomes (in terms of QALYs) over each of the modelled time horizons. Adopting a two-year time horizon costs for the surgical cohort are more than double the costs for the non-surgical cohort. However, as the time horizon increases, the absolute difference in costs between the surgical and non-surgical

cohorts remains more or less constant, and the proportionate difference reduces. Costs for the two cohorts increase, as the result of the need to maintain follow-up of both surgically and non-surgically treated patients and also because of the increasing proportion of each cohort with Type 2 diabetes. This was assumed to be approximately 5%, based on BMI-specific prevalence of Type 2 diabetes reported in the *Health Survey for England 2003*,[17] where diabetes prevalence in the population with a BMI between 30 and 35 was 7.21% for males and 4.71% for females. By the end of the 20-year time horizon prevalence of Type 2 diabetes was estimated at 15.4% in the non-surgical cohort and 13.8% in the surgical cohort.

The total discounted QALYs with surgical management are greater than with non-surgical management for each of the time horizons modelled, with the incremental gain increasing with increasing time horizon. For the longest time horizon (20 years) the majority of the QALY gains for the surgical cohort are realised in the first 10 years – these are the utility gains from reduced weight. In the base-case weight in the surgical cohort is assumed to revert to baseline level at around eight years following surgery – utility gains following this are the result of the lower proportion of patients with Type 2 diabetes and a lower proportion with CVD.

Cost-effectiveness of bariatric surgery (adjustable gastric banding) for moderate obesity (BMI ≥30 and < 35) – deterministic sensitivity analysis

A series of one-way sensitivity analyses were conducted for each time horizon. These are reported in *Table 73*. Scenarios considered in the sensitivity analysis include:

TABLE 72 *Total discounted and incremental costs, total discounted and incremental QALYs and ICERs for bariatric surgery (adjustable gastric banding) and non-surgical management of moderate obesity(BMI ≥30 and < 35), adopting varying model time horizons*

| | Model time horizon | | | | | | | | |
| | **2 years** | | | **5 years** | | | **20 years** | | |
	Non-surgical	**Surgical**	**Difference**	**Non-surgical**	**Surgical**	**Difference**	**Non-surgical**	**Surgical**	**Difference**
Cost (£)	3484	8403	4919	4503	9393	4890	9311	14,398	5087
QALY	1.62	1.70	0.08	3.74	4.03	0.30	11.12	11.52	0.40
ICER (£)			60,754			16,381			12,763

ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

TABLE 73 *Deterministic sensitivity analysis for cost-effectiveness of surgical management of moderate obesity (BMI ≥ 30 and < 35)*

	Model time horizon								
	2 years			**5 years**			**20 years**		
	Incr. cost (£)	Incr. QALYs	ICER (£)	Incr. cost (£)	Incr. QALYs	ICER (£)	Incr.cost (£)	Incr. QALYs	ICER (£)
Base case	4919	0.08	60,754	4890	0.30	16,381	5087	0.40	12,763
Health state utility (0.0075 gain per unit reduction in BMI)	4919	0.04	131,229	4890	0.14	35,322	5087	0.20	25,247
Operative mortality (0.1%)	4917	0.08	62,012	4887	0.29	16,595	5079	0.39	13,122
Operative mortality (0.05%)	4919	0.08	60,754	4890	0.30	16,381	5087	0.40	12,763
Band adjustments in second year (4)	5532	0.08	68,329	5503	0.30	18,436	5700	0.40	14,302
Band adjustments third year (2)	6993	0.08	86,370	6964	0.30	23,329	7161	0.40	17,967
Surgeon experience: increase duration of surgery (50%) and double revision rates	6996	0.04	188,545	6986	0.17	40,016	7346	0.22	33,058
Surgeon experience: reduce estimated weight loss by 25%									
Increase cost of preoperative assessment by 20%	5142	0.08	63,505	5113	0.30	17,128	5310	0.40	13,322
Increase operative cost by 20%	5890	0.08	72,745	5861	0.30	19,634	6058	0.40	15,199
Increase postoperative costs by 20%	5266	0.08	65,040	5408	0.30	18,117	6205	0.40	15,569
Increase all costs by 20%	6460	0.08	79,783	6602	0.30	22,115	7399	0.40	18,563
Reduction in SBP (increase by 50% for surgical patients)	4919	0.08	60,694	4889	0.30	16,340	5087	0.40	12,570
Reduction in TC:HDL ratio (increase by 50% for surgical patients)	4919	0.08	60,673	4890	0.30	16,329	5090	0.40	12,530
Reduction in SBP and TC:HDL ratio (increase by 50% for surgical patients)	4919	0.08	60,627	4889	0.30	16,296	5089	0.41	12,368
Reduce diabetes health state cost by 50%	4965	0.08	61,319	5032	0.30	16,856	5461	0.40	13,701
Reduce costs of health-service contacts for patients on intensive programme by 50%	6174	0.08	76,254	6162	0.30	20,643	6359	0.40	15,955
Increase costs of health service contacts for patients on intensive programme by 50%	3664	0.08	45,255	3618	0.30	12,120	3815	0.40	9571

BMI, body mass index; ICER, incremental cost-effectiveness ratio; Incr., incremental; QALYs, quality-adjusted life-years; SBP, systolic blood pressure TC:HDL, total cholesterol to high-density lipoprotein ratio.

- reducing the change in utility associated with a unit change in BMI (from 0.0166 to 0.0075)
- including a low operative mortality for surgery (rather than zero, as applied in the base case)
- allowing band adjustments in the second and/or third year rather than four only in year one
- considering the impact of surgeon inexperience – on duration of surgery, on revision rates and on outcome (in terms of weight reduction)
- increasing elements of surgical cost by 20%
- varying costs of health-service contacts for patients on the intensive programme
- considering the impact on reducing health-state costs for diabetes.

In all cases the least favourable ICERs are associated with a short model time horizon, ranging from around £45,000 per QALY gained up to £190,000 per QALY gained. More favourable ICERs are found for the five-year and 20-year time horizons, ranging from around £16,000 per QALY gained up to £40,000 per QALY gained for five-year time horizon and from around £12,500 per QALY gained up to £33,000 per QALY gained for the 20-year time horizon. In some scenarios, even for longer time horizons, the ICERs are above the range conventionally deemed as cost-effective from an NHS decision-making perspective.

In general the results are robust to changes in assumptions. However, changes in some key assumptions produce less favourable cost-effectiveness estimates than the base case adopted for this analysis.

- Applying a lower utility gain for reduction in BMI has a large impact on the QALY gain associated with surgery, reducing from 0.08 to 0.04 at two years (applying a utility gain per unit BMI reduction of 0.0075, the value adopted in the previous review). This effect is maintained over the varying time horizons of the model, with the QALY gain being reduced by between 49% and 54%. The effect of this is to raise the ICER substantially so that it remains above conventionally acceptable cost-effectiveness thresholds until the time horizon extends to 20 years.
- Repeating the scenario analysis, described earlier, for surgical experience leads to increased costs (because of increased duration in surgery and increases in the rate of revision) and poorer outcomes (i.e. reduced QALYs as the result of lower weight reduction).

The effect of these altered assumptions is shown cumulatively, with the effects on costs considered first. Increasing duration of surgery and revision rates leads to an increase in incremental costs of approximately £2000. The ICER increases to £86,370 at two years and £17,967 at 20 years. Reducing estimated weight loss by 25% reduces the QALY for surgical management by around 0.04 QALYs at two years and 0.18 QALYs at 20 years (approximately 54% and 44% reduction respectively) resulting in an ICER of £188,545 at two years and £33,058 at 20 years.

- Increasing operative costs by 20% increases incremental costs for surgery by approximately £1000, increasing the ICER at two years to £72,745 (£15,199 at 20 years). Increasing postoperative costs by 20% increases incremental costs by approximately £350, increasing the ICER to £65,040 at two years and £15,569 at 20 years. Increasing all surgery-related costs by 20% leads to an increase in incremental costs increasing by approximately £1500, increasing the ICER to £79,783 at two years and £18,563 at 20 years.
- Variation in the cost of health service contacts for patients on the intensive medical programme has a relatively large impact on incremental costs as these comprise a substantial proportion of the total costs of the intensive medical programme. Reducing costs of contacts by 50% increases incremental costs by approximately £1300 and increases the ICER at two years to £76,254 (£15,955 at 20 years). Conversely, increasing costs of contacts by 50% reduces incremental costs by approximately £1300 and reduces the ICER at two years to £45,255 (£9571 at 20 years).

Cost-effectiveness of bariatric surgery (adjustable gastric banding) for moderate obesity (BMI ≥30 and < 35) – probabilistic sensitivity analysis

In a probabilistic sensitivity analysis, where percentage weight loss, reduction in systolic blood pressure and TC : HDL ratio, proportion of patients with remission of Type 2 diabetes, health-state utility, health-state costs and costs of health service contacts for non-surgical patients during the intensive medical programme were sampled probabilistically, all simulations produced incremental cost-effectiveness estimates that were in the north-east quadrant of the cost-effectiveness map (*Figure 7*, which also shows the 95% confidence ellipses for the ICER).
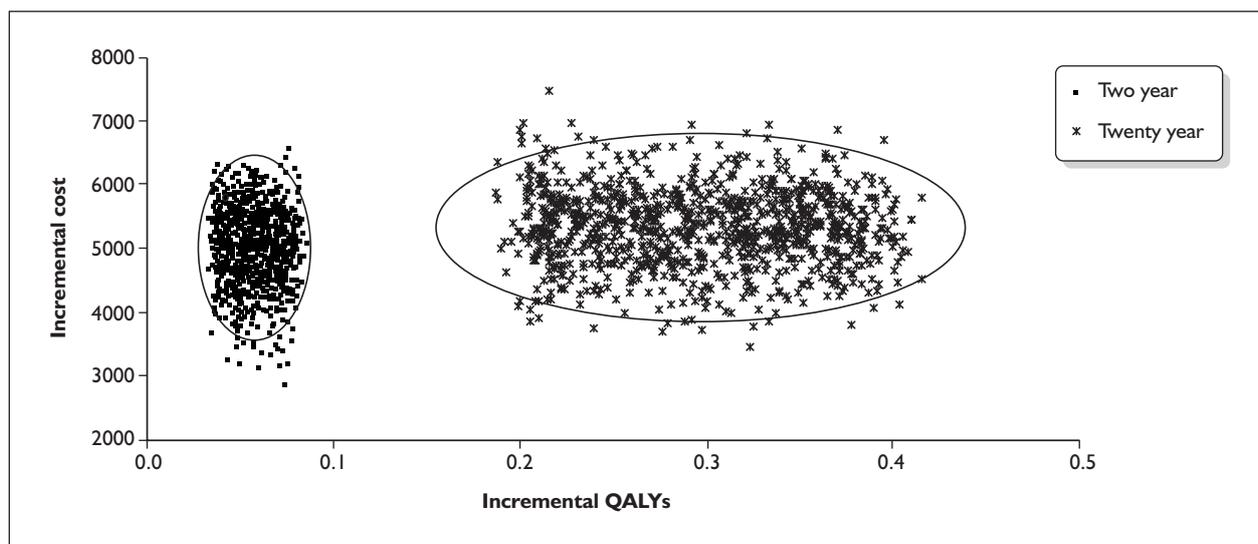
FIGURE 7 *Cost-effectiveness plane – incremental costs and incremental QALYs for patients with moderate obesity (BMI ≥30 and < 35), undergoing adjustable gastric banding compared with an intensive medical programme. QALYs, quality-adjusted life-years.*

In this analysis, surgical management with adjustable gastric banding had a probability of being cost-effective (compared with the intensive medical programme) of 64% at a willingness-to-pay threshold of £20,000 per QALY and 98% at a willingness-to-pay threshold of £30,000 per QALY for a time horizon of 20 years (*Figure 8*). In contrast the probability of surgical management being cost-effective was zero at both willingness-to-pay thresholds, when adopting a time horizon of two years (i.e. when using data from the clinical trial report[115] with no extrapolation of outcomes).

Discussion of cost-effectiveness
Summary of key results

- We reviewed the economic model developed for the previous assessment report and identified a number of potential updates that could be applied in this report:
  - The conceptual model (including health states for non-diabetic, postdiabetic and diabetic patients as well as death) was extended to include CHD and stroke. Methods relevant to modelling the incidence of CHD and stroke in obese
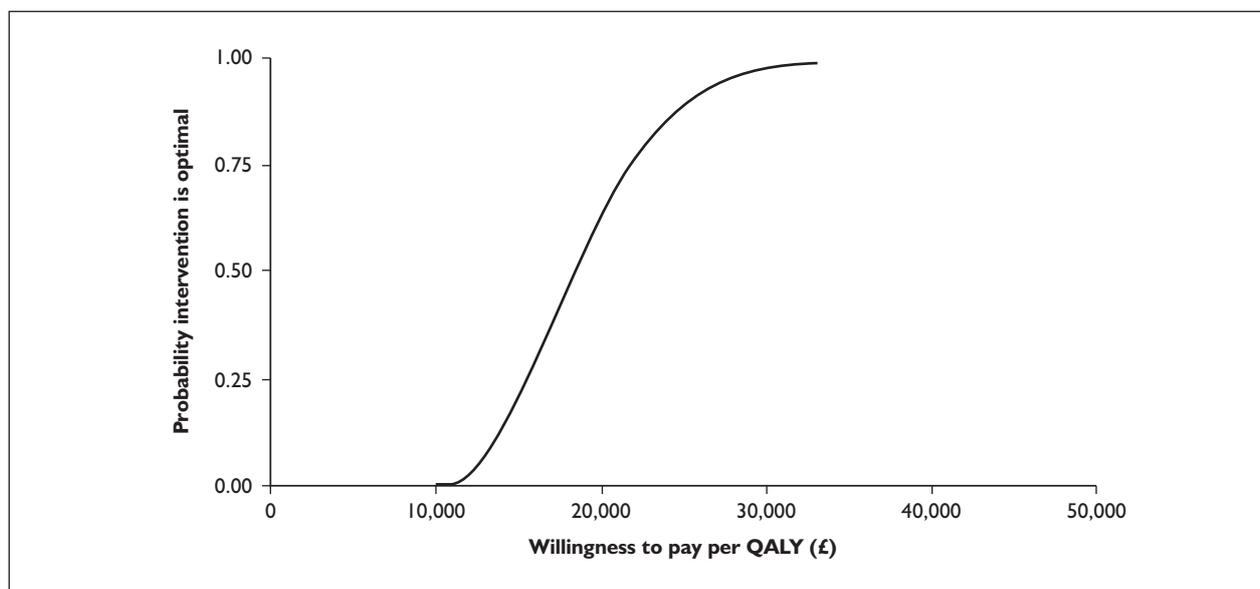
FIGURE 8 *Cost-effectiveness acceptability curve for adjustable gastric banding in patients with moderate obesity (BMI ≥30 and < 35) using a 20-year time horizon. QALY, quality-adjusted life-year.*

and Type 2 diabetes populations were investigated.
- Updated estimates of the utility impact of weight reduction were incorporated, including estimates of the impact of comorbidity.
- BMI-specific diabetes incidence estimates were incorporated into the model as well as estimates of the impact of weight reduction on the development of cardiovascular comorbidities.
- Expert opinion suggested that resource use assumptions adopted in the previous report, for costing bariatric surgery, did not reflect current practice in the UK. Updated resource use assumptions were developed, based on review of the literature, discussion with surgical specialists and a costing developed by a specialist service.
- While the conceptual model was extended to include CHD and stroke, it was recognised that appropriate parameter inputs to include these comorbidities may not be available for all modelled populations. In this situation an updated version of the model used in the previous assessment report (updated for cost and utility estimates) would be adopted.
- The analysis was developed for three patient populations covered by studies included in the clinical effectiveness review:
  - patients with morbid (Class III, BMI ≥40) obesity – as in the previous review;
  - patients with moderate to severe (Class I to Class II, BMI > 30 and < 40) obesity with significant comorbidity at baseline (Type 2 diabetes) undergoing laparoscopic adjustable gastric banding or receiving conventional therapy, based on data from a single trial[117]
  - patients with moderate (Class I, BMI ≥30 and < 35) obesity undergoing laparoscopic adjustable gastric banding or an intensive medical programme, based on data from a single trial.[115]
- Included trials for patients with morbid obesity did not report measures of cardiovascular risks that were suitable for our new model. Hence the model developed for the previous assessment report was used for this population. The economic model adopted 'optimistic' estimates (based on the previous assessment report) and an alternative 'pessimistic' estimate (based on a recently published trial[107] comparing gastric bypass and gastric banding), as the clinical effectiveness review concluded

that meta-analysis was not appropriate. Weight loss outcomes were extrapolated to 10 years following surgery based on long-term outcomes reported for the SOS study.[97] In the absence of a robust, pooled estimate of treatment effect (with associated estimate of variability) we felt it was inappropriate to undertake probabilistic sensitivity analysis for the model applied to patients with morbid obesity.
- The clinical trials reporting the use of adjustable gastric banding for moderate-to-severely obese (BMI ≥30 and < 40) patients with Type 2 diabetes and for moderately obese (BMI ≥30 and < 35) patients reported sufficient information, up to two years of follow-up, to apply the new model. The time horizon for these analyses was initially for the period of the trial follow-up only. However, extrapolations based on data from the SOS study (where relevant) or on the basis of data reported in the trial were undertaken.

Cost-effectiveness of bariatric surgery (gastric bypass or adjustable gastric banding) for morbid obesity (BMI ≥40)
- Surgical management of morbid obesity with gastric bypass or adjustable gastric banding is estimated to be more costly than non-surgical management, but results in improved outcomes (in terms of QALYs) over the modelled 20-year time horizon. Using the optimistic assumption on weight reduction up to five years following surgery the QALY gain for adjustable gastric banding is 1.88, while using the pessimistic assumption the QALY gain is 0.92. The equivalent values for gastric bypass are 1.98 and 1.52 QALYs. These QALY gains are larger than those estimated in the previous report, because of extrapolation of effects over 10 years (rather than the assumption of immediate reversion to baseline weight at five years) and updated assumptions on the utility gain associated with a unit reduction in BMI. The ICERs range between £1897 and £4127 per QALY gained.
- The results were generally robust to changes in assumptions in the deterministic sensitivity analysis, and in all cases the ICERs remained within the range conventionally regarded as cost-effective from an NHS decision-making perspective. Some key assumptions produced less favourable cost-effectiveness estimates – in particular reducing the utility gain associated with a weight loss to the value used in the previous review, and adopting alternative, less favourable assumptions (longer duration

of surgery, higher revision rates and lower weight loss) that might be associated with less experienced surgical operators.

Cost-effectiveness of bariatric surgery (adjustable gastric banding) for moderate to severe obesity (BMI ≥30 and < 40) in patients with Type 2 diabetes

- Results were reported for three time horizons: two years (corresponding to the duration of the clinical trial report), five years and 20 years [by which time it was assumed all patients had reverted to baseline weight, systolic blood pressure and TC : HDL ratio, and that all patients who resolved Type 2 diabetes (following surgery or through conventional treatment) had relapsed]. For each time horizon, surgical management of moderate to severe obesity in patients with Type 2 diabetes is estimated to be more costly than non-surgical management, but results in improved outcomes. The QALY gain of 0.27 at two years, increases to 1.10 for the 20-year time horizon. Incremental costs reduced from £5032 at two years to £1500 for the 20-year time horizon. The reduction in incremental cost arises from the difference in Type 2 diabetes resolution between the two modelled cohorts, with 73% of surgically treated patients resolving Type 2 diabetes at two years of follow-up (relative risk, compared with non-surgical patients, of 5.5, 95% CI 2.2 to 14.0).[117] The ICER reduced with longer time horizon from £18,930 at two years to £1367 at 20 years.
- The results were generally robust to changes in assumptions in the deterministic sensitivity analysis. However, some key assumptions produced less favourable cost-effectiveness estimates – in particular reducing the diabetes health-state cost, assuming a gradual (rather than immediate) reduction in weight following surgery, reducing the utility gain associated with weight loss to the value used in the previous review, and adopting alternative, less favourable assumptions (longer duration of surgery, higher revision rates and lower weight loss) that might be associated with less-experienced surgeons. The impact of these changed assumptions was particularly marked for the two-year time horizon.
- In the probabilistic sensitivity analysis all simulations were associated not only with increased QALYs, but also increased costs, when adopting a two-year time horizon. However, when the time horizon was extended to 20-years, while all simulations showed

increased QALYs a proportion had negative incremental costs (total discounted costs for the surgical cohort were lower than for the non-surgical cohort). These occurred in simulations where surgical treatment was associated with high proportions of patients with remission of Type 2 diabetes. With a two-year time horizon the probability of surgical management being cost-effective (compared with non-surgical management) was 2.5% at a willingness-to-pay threshold of £20,000 per QALY and 50.6% at a willingness-to-pay threshold of £30,000 per QALY, assuming a gradual reduction in weight following surgery. In contrast the probability of surgical management being cost-effective was 100% at both willingness-to-pay thresholds, for a 20-year time horizon.

Cost-effectiveness of bariatric surgery (adjustable gastric banding) for moderate (BMI ≥30 and < 35) obesity

- Results were reported for three time horizons: two years (corresponding to the duration of the clinical trial report), five years and 20 years. For each time horizon, surgical management of moderate obesity is estimated to be more costly than non-surgical management, but results in improved outcomes. The QALY gain of 0.08 at two years, increases to 0.40 for the 20-year time horizon. Incremental costs are approximately £5000 for each time horizon. The ICER reduced with longer time horizon – from £60,754 at two years to £12,763 at 20 years.
- In the deterministic sensitivity analysis the least favourable ICERs were associated with short model time horizon, ranging from around £60,000 per QALY gained up to £190,000 per QALY gained. More favourable ICERs were found for the five and 20-year time horizons, ranging from around £16,000 per QALY gained up to £40,000 per QALY gained for the five-year time horizon and from around £12,500 per QALY gained up to £33,000 per QALY gained for the 20-year time horizon. In some scenarios, even for longer time horizons, the ICERs are above the range conventionally deemed as cost-effective from an NHS decision-making perspective – in particular reducing the utility gain associated with a weight loss to the value used in the previous review, and adopting assumptions that might be associated with less experienced surgeons were associated with high ICERs for all time horizons.
- In the probabilistic sensitivity analysis all simulations were associated with increased

QALYs but also increased costs, for all time horizons. With a 20-year time horizon the probability of surgical management being cost-effective (compared with an intensive medical programme) was 64% at a willingness-to-pay threshold of £20,000 per QALY and 98% at a willingness-to-pay threshold of £30,000 per QALY. In contrast, the probability of surgical management being cost-effective was zero at both willingness-to-pay thresholds, for a two-year time horizon.

Generalisability

- In general, the clinical trials used to model the effectiveness of bariatric surgery for morbidly obese (BMI ≥40) patients reflect the key characteristics of the population discussed in Chapter 1, Description of Health problem, with the majority of patients recruited to the trials being female. These trials also generally recruit patients meeting the eligibility specified by current NICE guidance, with inclusion criteria specifying a BMI > 40, or a BMI > 35 for patients with significant comorbidity. An exception to this, is the trial reported by O'Brien and colleagues,[115] which recruited patients with moderate obesity (BMI ≥30 and < 35), below the threshold for weight loss surgery adopted in current clinical guidelines.[9,146] The majority of patients recruited to the trial also seemed to be free of major comorbidities associated with obesity. In addition, in those trials recruiting patients meeting current clinical criteria for weight loss surgery (in terms of BMI) it is not always clear from the trial reports, what previous weight loss regimes the patients have undergone and whether they failed to achieve and maintain weight loss with non-surgical management (as specified in the NIH[146] and NICE guidance[9]).
- Some of the included trials specified inclusion criteria in relation to patient age – for example Angrisani and colleagues[107] recruited patients between the ages of 16 and 50 years, van Dielen and colleagues[127] recruited patients between 18 and 60 years, Lee and colleagues[124] recruited patients between 18 and 59 years, while Howard and colleagues[120] recruited patients below 50 years of age. The lower age criteria relate to distinctions between adult and adolescent/paediatric services. However, it is more likely that the upper age limits reflect issues in the design of the clinical trials (for example, to recruit patients whose comorbidities are more likely to be obesity-

related rather than age-related) rather than the expected patient group for bariatric surgery.

- The patient population in the trial reported by Angrisani and colleagues[107] was 83% female with a BMI between 35 and 50, without specifying the presence of comorbidities and therefore had inclusion criteria wider than the current NICE guidance, whereas in the trial reported by Nilsell and colleagues[126] the inclusion criteria specified a BMI of greater than 40, or greater than 37 with an obesity-related comorbidity. Inclusion criteria for the trial reported by Dixon and colleagues[117] were also wider than the current NICE guidance with moderate to severely obese patients with Type 2 diabetes – patients were included if their BMI was greater than 30 but less than 40.
- Clinical trials providing data used in the economic model were conducted in a variety of countries (Italy, Sweden and Australia). It is not clear how differences in clinical practice between countries are likely to influence the outcomes of procedures, nor the extent to which the results obtained in specialist centres conducting clinical trials can be generalised to other settings. Some of the included clinical trials (for example, Angrisani and colleagues[107]) refer directly to the impact of surgeon experience and the learning curve on patient outcomes – particularly with respect to the frequency of operative complications. To some extent this uncertainty is addressed in the analysis by considering a scenario where less-experienced surgeons are characterised by longer operative duration, higher operative mortality rates, higher rates of non-fatal complications and poorer outcomes (in terms of average weight loss).
- Expert opinion suggested that resource use estimates (in terms of duration of surgery and length of stay) extracted from included clinical trials were likely to overestimate resource use in the UK setting. Updated estimates were developed based on expert clinical opinion. However, these have not been validated against any external standard. Discussion with clinical experts suggested that there was likely to be considerable variation in surgical practice (for example, some centres may undertake prophylactic cholecystectomy on all patients, while others would not perform any cholecystectomies on bariatric surgery patients at the time of the initial operation) and in the involvement of clinical psychology (for example, some services may limit involvement to patients with documented psychological

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illness). The costings in the report are based, as far as possible, on implementation of NICE guidance and therefore assume that all patients have a psychological evaluation and continuing psychological support following surgery.

- As far as possible the economic analyses have used routinely available unit cost estimates–*NHS Reference Costs*[185] and *Unit costs of health and social care*.[177] As no appropriate reference cost exists for bariatric surgery we developed a resource use protocol, which was refined by clinical experts (as discussed above) and costed in consultation with the costing unit at Southampton University Hospitals NHS Trust. Similarly, as no cost estimates existed for non-surgical management, protocols were developed–based on the previous assessment report, for morbidly obese patients, and on details in the clinical trial reports[115,117]–and costed using appropriate UK unit costs. Details of the costing protocols are presented in the Data sources, Cost data section in this chapter. The accuracy and comprehensiveness of costing for non-surgical management in the trials reported by Dixon and colleagues[117] and O'Brien and colleagues[115] is dependent on the reporting of the interventions in the clinical trial reports.

Strengths and limitations

- The model adopted for the economic evaluation in this review is based upon a previously published model, developed for assessing the cost-effectiveness of bariatric surgery in a UK setting. The model has been extended, where possible, to include cardiovascular comorbidity, and has been updated with respect to duration of weight loss following bariatric surgery, the estimated utility gain associated with reduction in BMI, remission (and durability of remission) of Type 2 diabetes, resource use and health-care costs.
- Clinical evidence, in terms of weight reduction, revision rates and operative complications, were extracted from the RCTs included, and critically appraised in the clinical effectiveness review. Where necessary, these sources were supplemented with data from long-term cohort studies within the scope of the review. These were also critically appraised in the clinical effectiveness review. The main effectiveness parameter in the model, weight reduction, is an accepted primary aim of bariatric surgery, although not all included trials

were powered on a measure of weight loss (where sample size calculations were reported). For example, the trial reported by Dixon and colleagues[117] was powered to detect a 1% difference in HbA_{1c} and also powered for diabetes remission rates (expected values 60% in the surgical group and 20% in conventional therapy).

- The majority of the data included in the model are in the public domain. Where updated assumptions have been developed in the course of this review (for example, resource use assumptions) these have been clearly documented and are presented in the body of this report. The model structure, assumptions and data inputs are clearly presented in this report. This should facilitate replication and testing of model assumptions and analyses.
- Patient utility was related to the main effectiveness parameter in the model using a published estimate of the change in utility associated with a unit change in BMI. The utility model was based on health-state preferences expressed by subjects in an RCT of pharmacotherapy and dietary modification for the treatment of obesity. Subjects covered a wide range of BMI, including 76 (of 621) categorised as morbidly (Class III) obese. Health-state preferences were assessed using a visual analogue scale (VAS; anchored at 0 for death and 100 for perfect health) to rank participants' current health states. VAS scores were transformed to their equivalent time trade-off values using a published conversion method.[189] These time trade-off values were included in a multiple regression model to derive an estimate of the change in utility associated with a unit change in BMI, controlling for baseline utility age and sex. A review of health-state preference values, related to changes in BMI, concluded that these were the most methodologically sound published estimates to include in the model. The robustness of the results to assumptions regarding utility were addressed in a sensitivity analysis.
- Published economic evaluations of bariatric surgery for morbid obesity were reviewed to develop estimates of resource use associated with bariatric surgery. Duration of surgery, length of stay, ITU and/or HDU admissions were extracted from identified reports and compared with assumptions

developed for the previous report. Updated assumptions were discussed with clinical experts who felt that these overestimated the duration of surgery and length of stay in comparison with current UK practice. New resource use estimates were developed, based on expert opinion, and were costed in consultation with the costing unit at Southampton University Hospitals Trust.

- A review of previous economic evaluations of surgery for morbid obesity identified factors that were likely to be particularly influential on cost and outcome estimates. The impact of these factors was tested in deterministic sensitivity analyses.

- A weakness in the economic model is that we were not able to conduct a robust meta-analysis on outcomes. For the morbidly obese population the clinical effectiveness review concluded that meta-analysis was inappropriate because, for comparison of certain surgical procedures there was only one study, and where there was more than one RCT there was heterogeneity in patient groups, comparator treatments and in outcomes reported. An additional practical limitation was the fact that standard deviations (or data to calculate them) were not reported in the majority of studies. For moderate-to-severely obese (BMI $\geq$ 30 and < 40) patients with Type 2 diabetes and moderately obese (BMI $\geq$ 30 and < 35) patients there was only one included trial each, comparing adjustable gastric banding with non-surgical management. These trials had limited follow-up periods – two years each, with some loss to follow-up [12.5% (5/40) of patients in the non-surgical group were reported as lost to follow-up at two years in the trial reported by O'Brien and colleagues[115]]. For the morbidly obese (BMI > 40) population the analysis is primarily based on three trials (for surgery outcomes, in terms of weight loss, the 'optimistic' assumption uses data from one trial for adjustable gastric banding[126] and another for gastric bypass,[120] while the pessimistic assumption uses both arms of the trial reported by Angrisani and colleagues[107]), whereas the effectiveness of non-surgical management is modelled through assumption based on the control cohort reported in the SOS study.[97] In all cases the comprehensiveness of the analysis (for effects such as reoperation or complications) is dependent on quality and completeness of reporting. A similar caveat applies to the resource assumptions and costings based on clinical trial reports.

- The cost-effectiveness model applies utility values for reduction in BMI associated with surgical or non-surgical management of obesity, but takes no account of any utility impact of side effects or complications of interventions. The cost impact of complications resulting in admission to ITU or reoperation are estimated based on proportions reported in included trials – although, as noted in the clinical effectiveness review, reporting of adverse events and complications is variable between studies. Similarly, in the analysis of surgery versus non-surgical management of moderate obesity (BMI $\geq$ 30 and < 35), the impact of approximately 30% of non-surgical patients being intolerant to VLCD or orlistat (reported by O'Brien and colleagues[115]) is included in cost calculations, but there is no assessment of the impact of side effects on utility. Reporting of long-term adverse effects – such as frequent vomiting or flatulence – following surgery is variable and of limited duration in included trials (up to three years postsurgery). However, where reported, the proportion of patients reporting such effects are non-trivial (28.5% frequent vomiting,[129] 13–25% emesis and 13–22% flatulence[118]). The likely duration of the side effects is not clear nor is it apparent how far the impact of these effects may offset any utility gains from reduction in BMI alone.

- A potentially serious weakness in published utility models is an assumption of linear additivity, with respect to BMI or change in BMI – the effect of reduction in BMI (or absolute value of BMI in the model applied in the previous review) is assumed to be constant over the range of BMI values. Hakim and colleagues[152] reported investigating more complex functional forms, but opted for a simple model on the grounds of parsimony and that the more complex specifications failed to add significant explanatory power (assessed using the adjusted R^2). However, the simple linear model cannot exclude the possibility of estimating utility values outside the logical range (in particular

estimating values greater than one, where a large change in BMI is observed). An additional, implicit, assumption is that the utility change is independent of initial BMI or that it is independent of proximity to an 'ideal' or target BMI. Hakim and colleagues[152] conducted a subgroup analysis re-estimating the regression on patients with a BMI greater than or equal to 30, but did not report any analysis of potential interactions between utility gain from reduction in BMI and baseline BMI, proximity to the non-obese range (i.e. to BMI below 30) or to a target or 'ideal' value (such as BMI of 25).

– There is uncertainty over resource use and costs associated with surgical management. Costs associated with the surgical admission, used in the economic model, are based on resource use protocols developed using expert opinion. Published resource use protocols were regarded as overestimates, in terms of duration of surgery and length of stay, and as poor predictors of cost in the UK. However, it has not been possible to validate the updated cost assumptions against external standards, reflecting current UK practice. Similarly, assumptions over preoperative assessments and postsurgical follow-up have been based on protocols, informed by expert opinion. Costs for non-surgical comparators were based on brief resource use protocols included in clinical trial reports – as such, they are dependent on the comprehensiveness of coverage in the clinical trial reports.

– A major source of uncertainty in the economic model relates to the absence of reliable, long-term data on the effectiveness (in terms of sustained weight loss) and the need for operative revision and conversion to alternative weight-loss methods. Data on long-term outcomes from the SOS study were used to extrapolate from clinical trial outcomes to longer term outcomes for patients with morbid obesity (BMI > 40) and also for patients with moderate-to-severe obesity (BMI ≥ 30 and < 40) and Type 2 diabetes. However, the validity of applying these data may be questioned – for example, in the clinical trial reported by Dixon and colleagues[117] surgical patients were treated with adjustable gastric bands, while an unknown proportion of patients in the SOS study were treated with non-adjustable bands. It is not clear how changes in surgical techniques (or indeed in non-surgical management of obese patients) occurring over the duration of long-term cohort studies may affect the outcomes observed. On the other hand, it is unlikely that clinical trials – powered to detect differences in outcomes within two years – will be able to provide robust data on longer-term outcomes, even assuming complete follow-up. Surgical experts providing advice during this review have been particularly concerned about the absence of data on the proportion of patients who initially undergo adjustable gastric banding, but who will require reoperation and ultimately undergo conversion to gastric bypass in the longer term – estimated at approximately 30%. This has not been included in the economic evaluation because, while it would be relatively straightforward to include a range of possible costs for reoperation and conversion in the economic model, there are no data to model the effect on outcome of patients who undergo late conversion to gastric bypass following initial adjustable gastric banding.

Chapter 6

Assessment of factors relevant to the NHS and other parties

The prevalence of obesity is rising and the NICE commissioning guide for the bariatric surgical service[68] has suggested that the average number of people receiving bariatric surgery (in line with NICE guidance) for a standard PCT population of 250,000 should be 25 per year in five years time, which equates to more than a threefold increase compared with estimated levels in 2006. Expert opinion has suggested that this may be too low. Such increases may necessitate a step change in service provision.

It is likely that greater resources will be required in primary care because for people to meet NICE criteria for surgery they must first have tried all appropriate non-surgical measures, unless they have a BMI of 50 or over in which case surgery may be considered as a first-line option. Following surgery the management of any minor adverse events will also occur within primary care and GPs and practice nurses may need more training to recognise and manage some of these events appropriately.

Greater resources may be required to provide band adjustment services for people who have received a gastric band. At present, expert opinion suggests that the pattern of follow-up care is variable both in quality and quantity. Appropriate band adjustment may improve weight loss outcomes and have effects on utility and costs.

Chapter 7

Discussion

Statement of principal findings

Clinical effectiveness
Surgery versus non-surgical interventions
Weight loss

The surgical option has been shown to be the more effective intervention for weight loss in obese people in each RCT[115–117,119] and cohort study[102–104] comparing gastric bypass, adjustable gastric banding and biliopancreatic diversion with a non-surgical intervention, and in each cohort study[82–101,105] where participants received a different mix of surgical options. A variety of measures were used to report weight outcomes over different time spans. One RCT[117] reports a statistically significant difference in per cent initial weight lost after two years (laparoscopic adjustable gastric banding 20.0% ($\pm$ 9.4) versus 1.4% ($\pm$ 4.9) in the conservative therapy group, $p < 0.001$) and in kg of weight lost at two years. The statistical significance of the reported reduction in BMI and per cent excess weight loss at two years is not reported. Another RCT with a maximum follow-up of two years[115,116] reports statistically significant differences between the laparoscopic adjustable gastric banding and non-surgical group using four different outcome measures (weight in kg, BMI, per cent initial weight lost and per cent excess weight lost). In contrast, the third RCT[119] did not report a statistical comparison between biliopancreatic diversion and a dietary intervention but instead reported separately for men and women statistically significant reductions from baseline to one year for measures of weight, BMI, fat-free mass and fat mass in the biliopancreatic diversion group that were not apparent in the dietary group. The cohort study[102–104] that compared adjustable gastric banding and gastric bypass with a non-surgical intervention reported that BMI was statistically significantly lower two years after surgery [laparoscopic adjustable gastric banding 33.2 ($\pm$ 4.7) or open Roux-en-Y gastric bypass 32.9 ($\pm$ 6.7) versus control 41.0 ($\pm$ 3.4), $p < 0.001$]. Weight and total fat mass were also statistically significantly reduced in comparison to baseline in the laparoscopic adjustable gastric banding group whereas the reductions that occurred in the Roux-en-Y gastric bypass group

were not statistically significantly different. In the control group small increases that were not statistically significant occurred in both these measures after two years. The remaining two studies both compared a cohort that received different surgical interventions with a no surgery cohort[97,99,100,105] and reported a greater change in BMI after a mean of 3.2 years[105] and 10 years[97,99,100] following surgery. Absolute mean BMI values, although lower in the surgical cohorts, were not reported to be statistically significantly different in one study[105] and in the other a statistical comparison was not reported.[97,99,100] One study[105] reported one further weight loss outcome, finding that surgery led to a statistically significantly greater per cent excess weight loss after 3.2 years of follow-up. The other study[97,99,100] provides five further weight loss outcomes for this review update; surgery led to statistically significantly better outcomes in terms of per cent weight change and per cent BMI change after two years, and also weight and per cent weight change at 10 years. The difference in per cent weight change at 10 years was greater following surgery, but a statistical comparison with the control group is not reported.

HRQoL

There is evidence for improvement in some measures of HRQoL, particularly in the first couple of years following surgery. One RCT[115,116] provided evidence for a statistically significant improvement in five of the eight domains of the SF-36 (physical function, physical role, general health, vitality and emotional role) two years after laparoscopic adjustable gastric banding. Over longer time periods (up to 10 years) there is mixed evidence from a large cohort study[100] with statistically significantly greater change following surgery after 10 years observed in some HRQoL measures but not others.

Comorbidities

Surgical interventions led to greater improvements in comorbidities than non-surgical interventions. One RCT[117] specifically enrolled people with Type 2 diabetes and after two years found statistically significantly higher remission of the disease following laparoscopic adjustable gastric banding than conventional therapy (laparoscopic

adjustable gastric banding: 73% of participants with remission versus 13% in the conventional therapy group, $p < 0.001$) and statistically significantly fewer people with the metabolic syndrome. A large cohort study[96,97,136] has reported that after 10 years a statistically significantly greater proportion of people who had received surgery had recovered from diabetes, hypertension, hypertriglyceridaemia, low HDL-cholesterol and hyperuricaemia. Furthermore, in those without the relevant comorbidities at baseline, the incidence of diabetes, hypertriglyceridaemia and hyperuricaemia (but not hypercholesterolaemia) was statistically significantly lower in the surgical cohort than the control cohort.

Mortality, adverse events and complications

The commonly reported adverse events associated with the non-surgical interventions were intolerance to prescribed medications such as orlistat and metformin, or intolerance to a VLCD or meal replacement. These events can be resolved by discontinuing treatment. A further complication of rapid weight loss, which is also observed following surgical interventions, is cholecystitis which occurred in a greater proportion of people receiving conventional therapy than those receiving laparoscopic adjustable gastric banding in the single RCT that reported this outcome. However, a cohort study[96] reported that after two years obesity surgery statistically significantly increased the incidence of cholelithiasis and cholecystectomies in men, but that there was no difference in the incidence of these events among women.

Surgery versus other surgical interventions
Gastric bypass
Weight loss
Gastric bypass has been compared with four other surgical options and is reported to be more effective than adjustable gastric banding (one trial[107]), and more effective than vertical banded gastroplasty (statistically significant difference in three trials,[108,109,120,123] greater weight loss in the remaining four trials either not statistically significantly different[106,121,122] or no statistical comparison reported[73,124]). At five years, laparoscopic Roux-en-Y gastric bypass was statistically significantly better than adjustable gastric banding in terms of per cent excess weight loss, mean weight and mean BMI.[107] There were also statistically significantly fewer weight loss failures and more participants with a BMI < 30 following laparoscopic Roux-en-Y gastric bypass than adjustable gastric banding.[107] In the seven

trials that assessed gastric bypass and vertical banded gastroplasty surgery, greater weight loss was observed following gastric bypass using a variety of different measures. However, statistically significant differences in favour of gastric bypass were only reported by three trials,[108,109,120,123] and in two of these trials the statistically significant difference only applied to the per cent excess weight loss outcomes.[108,109,120] Statistical comparisons for the other weight loss outcomes were not reported. The trial comparing gastric bypass with laparoscopic sleeve gastrectomy[125] was inconclusive. Adjustable gastric banding, vertical banded gastroplasty and laparoscopic isolated sleeve gastrectomy are restrictive procedures. Weight loss with gastric bypass was not significantly different to that with banded gastric bypass (one trial[118]). There were no differences in weight loss in the four trials reporting on the open and laparoscopic approaches to gastric bypass surgery (four trials[112–114,130,131]).

HRQoL
The HRQoL of people with gastric bypass has been compared with that of people with vertical banded gastroplasty (one trial[124]). Twelve months after surgery HRQoL as measured by the GIQLI had significantly improved for all patients but gastric bypass patients scored significantly better than vertical banded gastroplasty patients on 14 of the 36 individual items that make up the GIQLI. Vertical banded gastroplasty patients scored significantly better than gastric bypass patients on only one item. HRQoL following either open or laparoscopic gastric bypass has also been reported (1 trial[113,114]) and after three years there were no significant differences in MAQoL or BAROS outcome scores.

Comorbidities
Two studies comparing gastric bypass with adjustable gastric banding (one trial[107]) and banded gastric bypass (one trial[118]) reported comorbidities. The numbers of participants with comorbidities were low and unevenly dispersed between the groups in the small trial that compared gastric bypass and adjustable gastric banding. Therefore it is not possible to determine whether one procedure has a greater impact on comorbidities than the other. After gastric bypass and banded gastric bypass there was no statistically significant difference in the proportion of patients experiencing resolution of the six reported comorbidities. There was no statistically significant difference in the improvement or resolution of eight out of 10 comorbidities that were reported on

following either open or laparoscopic gastric bypass (one trial[113,114]). For the other two comorbidities a statistically significant difference was found in improvement/resolution of dyslipidaemia in favour of open gastric bypass, and in improvement/resolution of osteoarthritis symptoms in favour of laparoscopic gastric bypass.

Mortality, adverse events and complications
Of the 10 studies comparing gastric bypass to another surgical option eight reported no deaths in either trial arm.[106–109,118,120–122,124,125] In one study[123] two deaths occurred among the 20 patients in the Roux-en-Y gastric bypass group (10%) and none in the vertical banded gastroplasty group. In one trial[73] one death occurred among the 77 patients enrolled in the study (1.3%), but the trial arm in which this death occurred is not stated (gastric bypass, or loop gastric bypass or gastric banding, the latter trial arm has not been reported in this review). Gastric bypass was associated with more early complications than laparoscopic adjustable gastric banding and vertical banded gastroplasty, but a level of late complications similar to vertical banded gastroplasty and similar or reduced reoperation rates compared to laparoscopic adjustable gastric banding or vertical banded gastroplasty respectively. There were no differences in complications between gastric bypass and banded gastric bypass. In the four trials that compared the open and laparoscopic approaches to gastric bypass surgery, two reported no deaths,[112–114] but deaths occurred in both the open (1/51, 2%) and laparoscopic (2/53, 3.8% although one reported to be unrelated to surgery) groups in one trial,[130] and in the laparoscopic arm of the fourth trial (1/30, 3%).[131] Conversion to open surgery ranged from 0 to 23%. Anastomotic stricture and reoperations were more frequent following the laparoscopic approach, but wound infections and hernias were more common after open surgery.

Vertical banded gastroplasty
Weight loss
Vertical banded gastroplasty has been compared with two other surgical options and found to be less effective than gastric bypass as discussed above. The results from the trials comparing vertical banded gastroplasty to adjustable gastric banding (three trials[110,126–128]) do not enable a conclusion to be drawn regarding which procedure leads to greater weight loss. One year after surgery greater improvements in weight (reported by one trial[126]), per cent excess weight loss (reported by two trials[110,127,128]) and BMI (reported by two trials[110,127,128]) were evident for vertical banded

gastroplasty. However, a statistical comparison was not presented for the one-year weight outcome[126] nor for one of the trials reporting one-year BMI outcomes.[127,128] A statistically significant difference at one year was reported by both trials reporting per cent excess weight loss[110,127,128] and one of the trials reporting one-year BMI.[110] After two years statistically significant differences in BMI and per cent excess weight loss were only apparent in one of the two trials reporting these outcomes.[127,128] There were no differences in weight loss between the open and laparoscopic approaches to vertical banded gastroplasty surgery (one trial[111]).

HRQoL
The HRQoL of people with a vertical banded gastroplasty has been compared with that of people with a gastric bypass (one trial) as discussed above.

Comorbidities
Vertical banded gastroplasty has been compared with one other surgical option, adjustable gastric banding (one trial[127,128]). Although the overall number of patients with comorbidity significantly decreased following both vertical banded gastroplasty and adjustable gastric banding there were no significant differences in improvements in comorbidities between the groups.

Mortality, adverse events and complications
Of the 10 trials comparing vertical banded gastroplasty to another surgical option six reported no deaths[106,108–110,120–122,124] and one reported no immediate deaths related to surgery.[126] Deaths occurred in two trials comparing vertical banded gastroplasty with gastric bypass as discussed above, and in one trial comparing vertical banded gastroplasty to adjustable gastric banding where two of the 50 participants undergoing vertical banded gastroplasty died (4%), whereas there were no deaths in the adjustable gastric banding group.[123,124] Vertical banded gastroplasty was associated with fewer early complications than gastric bypass and a similar or reduced level of late complications than gastric bypass and laparoscopic adjustable gastric banding respectively. There were fewer reoperations following vertical banded gastroplasty than with gastric bypass and adjustable gastric banding. GERD occurred more often after vertical banded gastroplasty than adjustable gastric banding. In the trial that compared the open and laparoscopic approaches to vertical banded gastroplasty there were no deaths. Surgery wound problems, pathological scars and hernias were more common following open surgery.

Adjustable gastric banding
Weight loss

Adjustable gastric banding has been compared with three other surgical options and found to be less effective than gastric bypass (one trial) as discussed above, and less effective than laparoscopic isolated sleeve gastrectomy (one trial[129]) for the three weight loss outcomes reported: per cent excess weight loss, weight loss and BMI decrease. In the comparison of adjustable gastric banding with vertical banded gastroplasty (three trials) the results were equivocal as already stated above. There were no differences in weight loss between the open and laparoscopic approaches to adjustable gastric banding surgery (one trial[132]).

HRQoL
None of the studies reporting on adjustable gastric banding included an assessment of HRQoL.

Comorbidities
Adjustable gastric banding has been compared with three other surgical options. Comorbidity outcomes in comparison with gastric bypass (one trial) and vertical banded gastroplasty (one trial) are discussed above. Only one comorbidity, GERD, was reported on in comparison to laparoscopic isolated sleeve gastrectomy (one trial[129]). At one year, GERD had resolved in a greater percentage of participants in the laparoscopic adjustable gastric banding group than the laparoscopic isolated sleeve gastrectomy group, but statistical significance was not reported.

Mortality, adverse events and complications
Of the five trials comparing adjustable gastric banding to another surgical option three reported no deaths and one reported no immediate deaths related to surgery. The only deaths reported occurred in one trial comparing adjustable gastric banding to vertical banded gastroplasty and these did not occur in the adjustable gastric banding group as noted above. Adjustable gastric banding was associated with more late complications and a greater level of revisional surgery than vertical banded gastroplasty. Adjustable gastric banding was also associated with gastrointestinal effects such as more frequent vomiting than in laparoscopic isolated sleeve gastrectomy. In the trial that compared the open and laparoscopic approaches to adjustable gastric banding there were no deaths. Open surgery for adjustable gastric banding involved a longer hospital stay and more readmissions than laparoscopic adjustable gastric banding. Incisional hernia also occurred following open adjustable gastric banding.

Laparoscopic sleeve gastrectomy
Weight loss

Laparoscopic sleeve gastrectomy was superior to adjustable gastric banding (one trial[129]), but similar to gastric bypass (one trial[125]), as noted above.

HRQoL
The studies reporting on laparoscopic sleeve gastrectomy did not include an assessment of HRQoL.

Comorbidities
Resolution of GERD following laparoscopic isolated sleeve gastrectomy was compared with adjustable gastric banding (one trial[129]) as reported above. Comorbidity was not fully assessed in the trial comparing laparoscopic sleeve gastrectomy with gastric bypass,[125] although diabetes resolved in both the patients who had this comorbidity at baseline (both were in the gastric bypass group).

Mortality, adverse events and complications
Laparoscopic isolated sleeve gastrectomy led to generally fewer gastrointestinal effects than laparoscopic adjustable gastric banding and no deaths were reported. Similarly, the trial reporting on the comparison between laparoscopic sleeve gastrectomy and LGBP reported no conversions to open surgery and no intraoperative or postoperative complications.

Banded gastric bypass
Weight loss
Banded gastric bypass did not result in a significantly different weight loss to gastric bypass (one trial).

HRQoL
The study reporting on banded gastric bypass did not include an assessment of HRQoL.

Comorbidities
After gastric bypass and banded gastric bypass there was no statistically significant difference in the proportion of patients experiencing resolution of the six reported comorbidities.

Mortality, adverse events and complications
No deaths were reported. The only gastrointestinal symptom score that was statistically different between the groups was the score for emesis, which was statistically significantly better in the non-banded gastric bypass group. However, the proportion of participants with food intolerance was statistically significantly higher in this group.

Cost-effectiveness
Published economic evaluations

Five original economic evaluations were assessed in this report. Four of these compared different types of bariatric surgeries with a non-surgical treatment [138,140–142] and one was an economic evaluation alongside a clinical trial.[139] All modelled economic evaluations[138–142] found the evaluated bariatric surgeries to be cost-effective in comparison to non-surgical treatment although the variability in estimates of costs and outcomes is large. The results of the economic evaluation alongside a clinical trial[139] were inconclusive.

The choice and the range of model parameter estimates used in sensitivity analyses were not justified. Nevertheless, with respect to the limited number of parameters used in the sensitivity analyses the results appear to be robust to parameter variations. However, Craig and Tseng[140] identified some subgroups of older and less obese men for whom an open gastric bypass may exceed the threshold of US$50,000 per QALY depending on the value of clinical effectiveness parameters.

The reported results should be interpreted with care:

- because the natural disease progression was not explicitly modelled in terms of probabilities of obesity-related diseases in any of the identified modelled economic evaluations
- because of the various methodological shortcomings in modelled economic evaluations[138,140–142] identified and explained in the relevant sections of Chapter 5.
- because of some of the assumptions used in modelled economic evaluations.

The most important concerns are summarised below:

- *Clinical evidence used to obtain the primary outcomes (weight reduction)*. In all four studies with modelled economic evaluations[138,140–142] the BMI values were taken from the published evidence; however, it does not appear that any study conducted a systematic literature search and evidence analysis. Two studies, Craig and Tseng[140] and Jensen and Flum,[141] used the outcomes from a single published source of evidence, which may affect the validity of the estimate of the differential weight loss in the alternative treatments and the generalisability of results. Generalisability of results is also impaired by the choice of evidence that applies

only to a subgroup of the obese population: the population of obese patients with Type 2 diabetes as in Ackroyd and colleagues[138] and white female patients who were obese at the age of 18 as in Jensen and Flum.[141]

- *Assumptions about the target population*. Craig and Tseng[140] and Salem and colleagues[142] have assumed that the cohort of obese patients with BMI > 40 have no comorbidities at the baseline, which may not be a realistic assumption.
- *Assumptions about the outcomes of bariatric surgeries*. Ackroyd and colleagues[138] implicitly assumed that there is no differential operative mortality and postoperative morbidity between the two surgeries and the non-surgical treatment comparator. This is not likely to be a realistic assumption. The same is also true with respect to the assumption of a zero weight gain over the modelled time horizon in patients in the non-surgical treatment arm in Ackroyd and colleagues,[138] Craig and Tseng[140] and Salem and colleagues.[142]
- *Utility estimates*. Utility estimates reported in Ackroyd and colleagues,[138] were also used in Craig and Tseng[140] and Salem and colleagues.[142] However, these are not likely to be unbiased estimates of the HRQoL because of the multiple methodological shortcomings in the way they were derived from the available data. In addition the source data relate to the general population whose health-related preferences may differ from those of the obese population.

In summary, it appears that the identified studies have not provided reliable and generalisable estimates of the incremental cost-effectiveness of bariatric surgeries in comparison to non-surgical treatment.

SHTAC economic model

- The model developed for the previous assessment report was assessed against other published models for completeness and relevance, and the conceptual model was extended to include CHD and stroke. Cardiovascular risks are typically estimated using variables other than body weight or BMI (such as blood pressure and cholesterol measurements, as well as patients' age, sex, smoking status), so the inclusion of these additional health states in the economic model depends on the methods adopted to estimate transitions to these states and the extent to

which appropriate measurements are reported in clinical studies.

- The analysis was developed for three patient populations covered by studies included in the clinical effectiveness review:
  - patients with morbid (Class III, BMI > 40) obesity – as in the previous review
  - patients with moderate to severe (Class I to Class II, BMI > 30 and < 40) obesity with significant comorbidity at baseline (Type 2 diabetes), based on data from a single trial[117]
  - patients with moderate (Class I, BMI ≥ 30 and < 35) obesity, based on data from a single trial.[115]

- All surgical patients in the latter two groups above underwent laparoscopic adjustable gastric banding. Therefore gastric bypass was only included in the economic model for patients with morbid obesity (BMI > 40).

- The relevance of the three populations to current clinical guidelines was considered. Patients in the first group (with morbid obesity) and a subgroup of the second group (those with BMI greater than 35 and significant comorbidity) are considered appropriate for weight loss surgery under current clinical guidelines[9,146] if they have failed to achieve sustained weight loss using other methods. Some clinical opinion suggests that patients with less severe obesity (BMI between 30 and 35) who have significant comorbidity that may respond to surgically induced weight loss (such as Type 2 diabetes), may be potential candidates for weight loss surgery. However, they emphasise that further research is required, with a clearer indication of the patient's overall cardiovascular risk rather than relying on BMI.[190] In all cases the clinical consensus seems to suggest that weight loss surgery would not be an appropriate option for patients with mild obesity in the absence of evidence of cardiovascular risk or other significant comorbidity (which appears to be the majority of the patient population in the trial reported by O'Brien and colleagues,[115] where, at baseline, no patients had coronary artery disease, 38% had metabolic syndrome and 20% had hypertension).

- Meta-analysis of included clinical data was considered inappropriate. This has implications for the economic model. We adopted two estimates of the effect of gastric bypass and gastric banding on weight loss for the morbidly obese population. The first

was an 'optimistic' scenario (based on the previous assessment report) and the second a 'pessimistic' scenario (based on a recently published trial[107] comparing gastric bypass and gastric banding). Outcomes, in terms of weight loss at five years following surgery, were extrapolated using data from the SOS study.[97]

- Effectiveness data, in terms of weight loss, from the clinical trials reporting the use of adjustable gastric banding for severely obese patients with Type 2 diabetes and for moderately obese patients were used directly in the model. The analysis was initially undertaken for the period of the trial follow-up only. Extrapolations of longer-term weight loss were undertaken based on data from the SOS study, where relevant, or on the basis of data reported in the trial.

- We reviewed recently published studies reporting estimates of change in utility associated with change in weight or change in BMI. There is large variation in the estimated change in utility associated with a unit change in BMI, which relates to differences in the characteristics of the populations studied, and may also relate to the number of covariates included in the analysis. For the base case in the economic model we adopted values estimated by Hakim and colleagues[152] as these were derived from an obese (rather than an overweight) population, attempted to derive appropriate time trade-off values, and explicitly controlled for baseline utility. However, one potential problem with adopting this model is the assumption of a linear relationship between change in utility and change in BMI, that may produce biased or unfeasible estimates for large changes in BMI or at the extremes of the BMI range. The economic model does not include any utility adjustments for patients experiencing adverse effects associated with surgical or non-surgical management, nor are any adjustments included for patients undergoing surgical revision of their initial procedure. A scenario is included in the deterministic sensitivity analysis to reduce the utility gain associated with reduction in BMI to the value adopted in the previous assessment report.

- Updated resource use assumptions, to reflect current UK practice, were developed, based on discussion with surgical specialists and a costing developed by a specialist service. These were costed in consultation with a local NHS costing unit, based within the Trust Finance Department.

Cost-effectiveness of bariatric surgery for morbid obesity (BMI > 40)

- Surgical management with gastric bypass or adjustable gastric banding of morbid obesity was more costly than non-surgical management, but resulted in improved outcomes (in terms of QALYs) over the modelled 20-year time horizon. Differences between the optimistic and pessimistic scenarios were greater for adjustable gastric banding than for gastric bypass. Using the optimistic assumption on weight reduction up to five years following surgery the QALY gain for adjustable gastric banding is 1.88, while using the pessimistic assumption the QALY gain is 0.92. The equivalent values for gastric bypass are 1.98 and 1.52 QALYs. These QALY gains are larger than those estimated in the previous report, because of extrapolation of effects over 10 years (rather than the assumption of immediate reversion to baseline weight at five years) and updated assumptions on the utility gain associated with a unit reduction in BMI. The ICERs ranged between £1897 and £4127 per QALY gained.

- Some alternative scenarios considered in the deterministic sensitivity analysis produced less favourable cost-effectiveness estimates – in particular reducing the utility gain associated with a weight loss to the value used in the previous review, and adopting less favourable assumptions (in terms of duration of surgery, revision rates and weight loss) that might be associated with less experienced surgical operators. However, the results were generally robust to changes in assumptions in the deterministic sensitivity analysis, and in all cases the ICERs remained within the range conventionally regarded as cost-effective from an NHS decision-making perspective.

Cost-effectiveness of adjustable gastric banding for moderate to severe obesity (BMI ≥ 30 and < 35) in patients with Type 2 diabetes

- Results were reported for time horizons of two years (corresponding to the duration of the clinical trial report), five years and 20 years. For each time horizon, surgical management of moderate to severe obesity in patients with Type 2 diabetes was more costly than non-surgical management, but resulted in improved outcomes. The QALY gain of 0.27 at two years, increased to 1.10 for the 20-year time horizon. Incremental costs reduced from £5032 at two years to £1500 for the 20-year time

horizon, because of the difference in Type 2 diabetes resolution between the two modelled cohorts. The ICER reduced with longer time horizon – from £18,930 at two years to £1367 at 20 years.

- The results were generally robust to changes in assumptions in the deterministic sensitivity analysis. However, reducing the diabetes health-state cost, assuming a gradual (rather than immediate) reduction in weight following surgery, reducing the utility gain associated with weight loss to the value used in the previous review, and adopting less favourable assumptions (in terms of duration of surgery, revision rates and weight loss) that might be associated with less-experienced surgeons, produced less favourable cost-effectiveness estimates. The impact of these changed assumptions was particularly marked for the two-year time horizon.

- In the probabilistic sensitivity analysis all simulations were associated with increased QALYs, but also increased costs when adopting a two-year time horizon. However, when the time horizon was extended to 20 years a proportion of simulations had negative incremental costs (total discounted costs for the surgical cohort were lower than for the non-surgical cohort). These occurred in simulations where surgical treatment was associated with high proportions of patients with remission of Type 2 diabetes. With a two-year time horizon the probability of surgical management being cost-effective (compared with non-surgical management) was 2.5% at a willingness-to-pay threshold of £20,000 per QALY and 50.6% at a willingness-to-pay threshold of £30,000 per QALY, assuming a gradual reduction in weight following surgery. In contrast, for a 20-year time horizon, the probability of surgical management being cost-effective was 100% at both thresholds.

Cost-effectiveness of adjustable gastric banding for moderate obesity (BMI ≥ 30 and < 35)

- Results were reported for time horizons of two years, five years and 20 years. For each time horizon, surgical management was estimated to be more costly than non-surgical management, but resulted in improved outcomes. The QALY gain of 0.08 at two years, increased to 0.40 for the 20-year time horizon. Incremental costs were approximately £5000 for each time horizon. The ICER reduced with longer time

horizon – from £60,754 at two years to £12,763 at 20 years.

- In the deterministic sensitivity analysis the least favourable ICERs were associated with short model time horizon, ranging from around £60,000 per QALY gained up to £190,000 per QALY gained. More favourable ICERs were found for the five and 20-year time horizons, ranging from around £16,000 per QALY gained up to £40,000 per QALY gained for the five-year time horizon and from around £12,500 per QALY gained up to £33,000 per QALY gained for the 20-year time horizon. In some scenarios, even for longer time horizons, the ICERs are above the range conventionally deemed acceptable from an NHS decision-making perspective – in particular, reducing the utility gain associated with a weight loss to the value used in the previous review and adopting assumptions that might be associated with less-experienced surgeons were associated with high ICERs for all time horizons.

- In the probabilistic sensitivity analysis all simulations were associated not only with increased QALYs but also increased costs, for all time horizons. With a 20-year time horizon the probability of surgical management being cost-effective (compared with an intensive medical programme) was 64% at a willingness-to-pay threshold of £20,000 per QALY and 98% at a willingness-to-pay threshold of £30,000 per QALY. In contrast, for a two-year time horizon, the probability of surgical management being cost-effective was zero at both thresholds.

Strengths and limitations of the assessment

This review has the following strengths.

- It is independent of any vested interest.
- It has been undertaken following the principles for conducting a systematic review. The methods were set out in a research protocol (Appendix 1), which defined the research question, inclusion criteria, quality criteria, data extraction process and methods to be employed at different stages of the review.
- An advisory group has informed the review from its initiation. The research protocol was informed by comments received from the advisory group and the advisory group has reviewed and commented on the final report.

- The review brings together the evidence for the clinical effectiveness and cost-effectiveness of bariatric surgery for obese people. This evidence has been critically appraised and presented in a consistent and transparent manner.

- An economic model has been developed de novo following recognised guidelines and systematic searches have been conducted to identify data for the economic model. The main results have been summarised and presented.

In contrast, this review also has certain limitations:

- Synthesis of the included studies was through narrative review. Although 26 eligible studies were identified either comparing surgery with no surgery or comparing different surgical procedures, in several cases only one study assessed a particular pair of interventions, for example gastric bypass versus adjustable gastric banding, or gastric bypass versus biliopancreatic diversion.

- Meta-analysis was deemed inappropriate. In cases where the same procedures are compared by several studies, limitations in the literature prevented us from proceeding with meta-analysis. The most common limitation in the literature is that SDs are not reported by the majority of studies. In addition, data such as exact *p*-values or CIs, which might have been used to calculate a standard deviation, are also not reported. Furthermore, there are often differences in the outcome measures reported by the studies, or differences in the patient groups. If these limitations had applied to a minority of the studies available for meta-analysis we would have considered using a standard technique to impute the missing standard deviations. For example, the comparison assessed by the greatest number of studies was gastric bypass versus vertical banded gastroplasty, which was assessed by seven RCTs. Five of these RCTs reported similar outcomes that could be combined in a meta-analysis, but only two reported any measure of variance. All five trials found greater weight loss with gastric bypass. Notably, the two studies that reported different outcome measures both found no statistically significant difference. To combine these five RCTs in a meta-analysis (if SDs could be obtained from the authors) would be inappropriate not only because a proportion of the evidence would be

ignored, but also because it would give undue weight to these procedures relative to other different surgical procedures that could not be combined in a meta-analysis.

- Despite conducting a wide ranging and systematic search of the literature we did not identify any studies that met the inclusion criteria and assessed bariatric surgery in young people. There were also only two studies that included adults with either Class I or Class II obesity (BMI ranges 30–34.99 and 35–39.99 respectively).

- Deaths, adverse events and some complications are generally rare events and therefore it is not likely that evidence presented here provides reliable estimates of the incidence of these rare events because most of the studies, particularly the RCTs, were of a limited size and duration. The proportion of deaths reported by the included studies within surgical cohorts or single surgical trial arms ranged from 0.25 to 10%. A recent systematic review and meta-analysis of mortality in bariatric surgery reports meta-analysis of total mortality at 30 days or less was 0.28% (95% CI 0.22 to 0.34) with restrictive operations having the lowest mortality.[191] The limited size and duration of the RCTs may have led to an underestimate of some of the more frequently encountered complications such as failure of gastric bands, e.g. due to band slip or erosion, complications that usually necessitate band removal. The SOS cohort study which has been ongoing for over a decade provides data for greater numbers of participants but is vulnerable to various kinds of bias. In addition, some RCTs compared different procedures with open surgery being undertaken for one intervention, and laparoscopic surgery for the other.

- The included studies provided insufficient information on surgeon experience for learning curve effects to be assessed in the comparisons of open versus laparoscopic surgeries.

- Owing to the time constraints of this review we were unable to contact the authors of the primary studies to request additional data. Although this might have provided some additional useful information, we cannot be certain that sufficient data would have been forthcoming to enable a meta-analysis, and it is unlikely that further details would have changed our conclusions.

- The utility model adopted for the base case maybe an over-simplification by assuming linear additivity, with respect to change in BMI.

The utility gain associated with a reduction in BMI (or conversely the utility loss associated with an increase in BMI) is assumed to be constant over the range of BMI values and therefore cannot exclude the possibility of estimating utility values outside the logical range. Moreover, the model does not allow for interactions between baseline BMI or proximity to a target or 'ideal' value, that may modify the effect of change in BMI on utility.

- The economic model applies utility values to the reduction in BMI associated with surgical or non-surgical management of obesity, but takes no account of any utility impact of side effects or complications of interventions. Reporting of long-term adverse effects following surgery is variable and of limited duration in included trials. However, where reported, the proportion of patients reporting such effects is non-trivial. The likely duration of the side effects is not clear, nor is it apparent how far the impact of these effects may offset any utility gains from reduction in BMI alone.

- Costs associated with the surgical admission in the economic model are based on resource use protocols developed using expert opinion. Published resource use protocols were regarded as overestimates, in terms of duration of surgery and LOS, and as poor predictors of cost in the UK. However, it has not been possible to validate the updated cost assumptions against external standards, reflecting current UK practice. Similarly, assumptions over preoperative assessments and postsurgical follow-up have been based on protocols, informed by expert opinion. Costs for non-surgical comparators were based on brief resource use protocols included in clinical trial reports – as such, they are dependent on the comprehensiveness of coverage in the clinical trial reports.

- A major source of uncertainty in the economic model relates to the absence of reliable, long-term data on the effectiveness (in terms of sustained weight loss) and the need for operative revision and conversion to alternative weight loss methods. Data on long-term outcomes from the SOS study were used to extrapolate from clinical trial outcomes to longer-term outcomes. However, the validity of applying these data may be questioned – for example, a proportion of patients in the SOS study were treated with non-adjustable bands, which would not be considered an acceptable strategy in current practice. It is not

clear how changes in surgical techniques (or indeed in non-surgical management of obese patients) occurring over the duration of long-term cohort studies may affect the outcomes observed.

Other relevant factors

- This review updates a previous Technology Assessment Report[15] and Cochrane review.[70,71] The criteria for this updated review were broadened to include adults and young people with Class I and Class II obesity, as well as those considered to be morbidly obese (Class III obesity). To maintain the relevance of the review to current practice the historical procedures of horizontal gastroplasty and jejunoileal bypass have been excluded from this updated review.

- The duration of the majority of the studies included in this review lay between one and three years with, in general, very few dropouts reported or apparent from the shortest studies. However, it was reported or apparent from the results of the few studies with durations of four to six years that only a half to one-quarter of the study population contributed outcome data at the final time points.

- Only five (three RCTs, two cohort studies) of the studies included in this review reported any assessment of QoL issues. It is therefore difficult to make any judgement about the impact of weight loss interventions on the quality of an obese person's daily life.

- It was beyond the remit of this research to assess the impact of preintervention and postintervention education, counselling and support on the outcomes of the interventions. However, the majority of the studies included in this review did not provide such details, which may be important for understanding patient compliance with the lifestyle and diet modifications that are necessary for successful weight loss maintenance.

- Few studies included participants aged over 60 years, so it is uncertain how generalisable these results are to older adults.

- Most study participants were women, so it is uncertain how generalisable the results are to men.

- All the studies included in this review were conducted in countries other than the UK. It is difficult to determine how generalisable the results of the included studies are to the ethnically diverse population within the UK.

- Only two RCTs assessed sleeve gastrectomy and none of the included studies assessed a two-stage approach to gastric surgery for obesity using sleeve gastrectomy before another bariatric procedure. We are therefore not able to draw any conclusion regarding the use of a two-stage approach.

- The relatively short duration of the majority of the RCTs available for inclusion in this review may mean that the impact of late complications (such as gastric ulcers, stomal stenosis and erosions, and band slippage) and the need for revisional surgery are underestimated.

- Expert opinion indicates that vertical banded gastroplasty is almost never undertaken now. However, this procedure forms the bulk of the evidence base, reported by 11 of 20 comparisons of surgical procedures and one of the six comparisons with non-surgical interventions. Similarly, the bariatric procedures in common use are mainly undertaken laparoscopically now, but the available evidence includes a number of trials that include open procedures.

- In common with earlier versions[15,70,71] of this review, bariatric surgery interventions were found to be more effective than any of the non-surgical interventions in terms of weight loss and improvements in comorbidities. The longer-term information from one cohort study that is now available on quality of life (up to 10 years) provides mixed evidence with some HRQoL measures showing significantly greater change after surgery, but not others. Only two comparisons, gastric bypass versus vertical banded gastroplasty, and vertical banded gastroplasty versus adjustable gastric banding, are common to both our previous reviews[15,70,71] and this review. Gastric bypass continues to appear more effective for weight loss than vertical banded gastroplasty because three trials report statistically significant greater weight loss and greater weight loss is apparent in the remaining four trials although this loss is either not statistically different or no statistical comparison is reported. Data on comorbidities were not assessed in these trials. Three trials contributed evidence to the comparison of vertical banded gastroplasty versus adjustable gastric banding and the results continue to be conflicting regarding which procedure leads to greater weight loss. There was no new information to include on comorbidities for this comparison. There was no new information to include on QoL for either the gastric bypass versus vertical banded

gastroplasty or the vertical banded gastroplasty versus adjustable gastric banding comparisons.

- It has not been possible for us to determine how similar the results of this review are to the results of reviews of bariatric surgery undertaken by other authors because these have generally focused on one particular surgical intervention, and/or have included study types other than RCTs and/or have included interventions that are no longer in current use. Therefore the results are not directly comparable.

Chapter 8
Conclusions

Implications for service provision

A NICE commissioning guide for the bariatric surgical service was produced alongside the NICE obesity guideline. The commissioning guide has estimated that the benchmark rate at five years for a bariatric surgical service is 0.01% per year (or 10 per 100,000 population).[68] This means that for a standard PCT population of 250,000, the average number of people receiving bariatric surgery (in line with NICE guidance) would be 25 per year in five years time. The commissioning guide indicates that this equates to more than a threefold increase compared with the current estimated rate of bariatric surgery commissioned by the NHS in 2006.

Suggested research priorities

- There continues to be a need for good-quality, long-term RCTs comparing different operative techniques for obesity that include an assessment of patient QoL. To enable future meta-analysis, RCT data should be comprehensively reported, ideally including more than one widely used outcome measure such as weight, per cent excess weight loss or BMI, and details of the standard deviation about the mean for each outcome reported.
- A comparison of procedures which combine restrictive and malabsorption components such as gastric bypass with the purely restrictive procedures in current use, particularly adjustable gastric banding, would be desirable as only two small RCTs contribute evidence on these comparisons. However, this may not be possible because expert opinion suggests that in practice severity of obesity and the presence of comorbid conditions determines which procedure is suitable for an individual patient.
- The evidence base for the clinical effectiveness of bariatric surgery for adults with Class I or Class II obesity is very limited. Similarly, no evidence to inform on the clinical effectiveness of surgical intervention for obesity in young people was found that met our inclusion criteria. Further good-quality RCTs are

required to provide clinical effectiveness and QoL evidence for these two groups. In addition, it is essential that any new research reports on the resolution and/or development of comorbidities such as Type 2 diabetes and hypertension so that the potential benefits of early intervention can be assessed.
- Assessing the risks of different bariatric procedures is hampered by a lack of consistency in the reporting of adverse outcomes. A core set of important adverse outcomes should be identified so that a standardised approach to describing adverse outcomes can be developed.
- It was beyond the remit of this review to assess the impact of preintervention and postintervention education, counselling and support on patients' understanding of the procedures and the consequences of undergoing surgery. The provision of postsurgical care, e.g. frequency and amount of band adjustment, was also beyond the remit of this review. As all of these aspects have the potential to affect the outcome of the intervention they should be reviewed. The impact that these aspects have on outcomes should be reviewed.
- In addition to good-quality, long-term RCTs, there is a need for good-quality, long-term cohort studies to:
  - identify reoperation for late complications following all bariatric procedures and conversion to gastric bypass for patients initially managed with gastric banding
  - identify the duration of remission, following surgical or non-surgical management, of comorbidities associated with obesity to determine whether this is primarily associated with durability of weight loss or with other prognostic factors
  - identify providers at different stages of the learning curve and to document the impact of experience on the safety, effectiveness and efficiency of surgery
  - identify resource use for patients during preoperative assessment, surgical admissions and postoperative management to develop robust costings for bariatric procedures.

- Current utility models indicate that reduction in BMI is associated with gains in utility. However, there is uncertainty over the magnitude of this gain. Further research is required to establish the utility gain associated with reduction in BMI, to establish the most appropriate functional forms (current models tend to assume linear additivity which may lead to infeasible values) and to investigate interactions between utility gain from reduction in BMI and baseline BMI, proximity to the non-obese range or to a target 'ideal' value. The research should also consider whether utility gains from reduction in BMI that are observed over the short-term, are maintained over the longer term.

- Current utility models relate gains in utility to change in BMI. Further research is required to investigate whether there are additional utility gains associated with the resolution of comorbidity following surgical or non-surgical management of obesity. Similarly, economic models of surgical or non-surgical management of obesity would be improved by including estimates of the QoL impact of the side effects of treatment. This would require more systematic recording and reporting of adverse effects, as well as additional research on their impact on patients' QoL and the extent to which these may offset quality of life gains associated with reduction in BMI.

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Contributions of authors

J. Picot (Research Fellow) developed the research protocol, drafted the background section, assisted in the development of the search strategy, assessed studies for inclusion, extracted data from and quality-assessed the included studies, synthesised evidence, drafted and edited the final report, and project managed the study; J. Jones (Principal Research Fellow) developed the research protocol, assisted with drafting the background section, assessed studies for inclusion, extracted data from and quality-assessed the included studies, synthesised evidence, developed the economic evaluation, and drafted the report; J.L. Colquitt (Senior Research Fellow) developed the research protocol, drafted the background section, assisted in the development of the search strategy, assessed studies for inclusion, extracted data from and quality-assessed the included studies, synthesised evidence, and drafted the report; E. Gospodarevskaya (Senior Research Fellow) developed the research protocol, assisted with drafting the background section, assessed studies for inclusion, extracted data from and quality-assessed the included studies, synthesised evidence, developed the economic evaluation, and drafted the report; E. Loveman (Senior Research Fellow) developed the research protocol, drafted the background section, assessed studies for inclusion, extracted data from and quality-assessed the included studies, synthesised evidence, and drafted the report; L. Baxter (Research Fellow) assessed studies for inclusion, extracted data from and quality-assessed the included studies, synthesised evidence, and drafted the report; A.J. Clegg (Professor/Director of SHTAC) developed the research protocol, drafted the background section, assessed studies for inclusion, extracted data from and quality-assessed the included studies, synthesised evidence, and drafted the report.

Associated Cochrane Review

The systematic review of clinical effectiveness is published as a Cochrane Review in the Cochrane Database of Systematic Reviews 2009, Issue 2 Cochrane Reviews are regularly updated as new evidence emerges and in response to comments and criticisms, and the Cochrane Database of Systematic Reviews should be consulted for the most recent version of the Review.

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Appendix 1
Protocol methods

Report methods for synthesis of evidence of clinical effectiveness

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'.[74]

Search strategy

The search strategies will be devised and tested by an experienced information scientist. The strategies will be designed to identify: (1) clinical effectiveness studies reporting on comparisons between different bariatric surgical techniques, and comparisons between bariatric surgery and non-surgical interventions for obesity; and (2) 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 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; and Biosis.

This work will update a previous assessment,[15] 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 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, before 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.

Inclusion and exclusion criteria
Patients
Inclusion criteria
- Adult patients fulfilling the standard definition of obese, i.e. people with a 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 30 kg/m^2.

Interventions
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.

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.

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; or change in obesity-related comorbidities.
- Data will also be extracted on perioperative and postoperative mortality and morbidity, revision rates for surgical procedures, change in obesity-related comorbidities and cost-effectiveness.

Exclusion criteria

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

Types of studies
Inclusion criteria

- 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.

Inclusion and data extraction process
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.

Data extraction strategy

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

Quality assessment

- Cohort studies will be assessed using criteria recommended by the NHS CRD (University of York).[74]
- RCTs will be assessed using the Cochrane criteria for judging risk of bias.[75] These criteria include consideration of the following factors:
  - sequence generation
  - allocation concealment
  - blinding of participants, personnel and outcome assessors
  - incomplete outcome data
  - selective outcome reporting
  - 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 Jefferson.[76]
- The checklist for assessing good practice in decision analytic modelling will be used for critically appraising any decision models identified.[77]

Methods of 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 ITT analyses. If a meta-analysis is appropriate it will be performed using REVIEW MANAGER (REVMAN) software.

Methods for synthesising evidence of cost-effectiveness

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).

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]
- the disease states or events that 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 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 are 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[185] and PSS[177] 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 (1) adult patients with a lower BMI who do not meet NICE criteria for bariatric surgery, and (2) 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.

Appendix 2
Literature search strategies

The databases searched for the 2008 update of this review are listed below, together with the full search strategies employed. Further information regarding the searches undertaken for the identification of studies in the original review and earlier updates is provided in Appendix 3

Database searched	Clinical effectiveness searches	Cost-effectiveness and QoL searches
Medline: 1996–2008	Restricted to 2004–2008	2001–2008
EMBASE	2004–2008	2001–2008
PreMEDLINE: In-Process & Other Non-Indexed Citations	2004–2008	2001–2008
Cochrane: includes Central, Dare, CDSR, and HTA databases	2004–2008	2001–2008
Web of Knowledge: Science Citation Index (SCI)	2004–2008	2001–2008
Web of Knowledge: ISI Proceedings	2004–2008	2004–2008
PsycInfo	2004–2008	2001–2008
CRD	2004–2008	2001–2008
BIOSIS	2008	2008
CINAHL	2004–2008	2001–2008
AMED	2004–2008	2001–2008
BNI	2004–2008	2001–2008

Searched for Ongoing Trials
UKCRN
National Research Register
Clinicaltrials.gov
Controlled clinical trials
Australian New Zealand Clinical Trials Registry

Clinical effectiveness

The MEDLINE search strategy for the clinical effectiveness section of the review is reproduced below. This was adjusted as necessary for cost-effectiveness searches and for searching the other electronic databases listed in the table above for both clinical effectiveness and cost-effectiveness literature (including quality of life information). Search strategies are available from the report authors on request. The MEDLINE database search was restricted to 2004–08. Citations identified by the search were added to a REFERENCE MANAGER database on 6 February 2008.

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)

Search strategy
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)
Update search run on 29 July 2008: number retrieved = 108

Reference lists

The reference lists of relevant trials and reviews identified were examined.

Other searches

Authors of included studies and relevant experts were contacted where possible in order to obtain additional references, missing data, unpublished trials and any ongoing trials. The authors of a systematic review of treatments for obesity[51] provided the results of hand searches of the following journals:

- *International Journal of Obesity* (1977 to 2000, volume 24, part 12);
- *Obesity Research* (1993 to 2001, volume 9, part 2);

- *Obesity Surgery* (1991 to 2001, volume 11, part 2);
- *American Journal of Clinical Nutrition* (1966 to 2000, volume 72, part 6);
- *Proceedings of the Nutrition Society* (1960 to 2000, volume 59, part 4);
- *Journal of Human Nutrition and Dietetics* (1988 to 2001, volume 14, part 1);
- *Journal of the American Dietetic Association* (1980 to 1990, volume 90, part 12)

Appendix 3

Identification of studies in the original review and updates

There are three previously published versions of this systematic review of bariatric surgery;[15,70,71] each differs slightly in the studies included as the review has evolved. This section explains how the review has evolved and notes the main differences between the reviews. A flow chart of the identification of studies at each stage can be seen in *Figure 9*.

Original review 2002[15]

For the first edition of this review 2707 citations were identified by the searches, of which 2631 were excluded and 76 were retrieved for detailed examination. Thirty-seven studies were then excluded.[15] Eighteen studies and one systematic review were included (reported in 39 publications). This version included jejunoileal bypass (an intervention that is no longer practised and is not included in subsequent versions of this review), and excluded abstracts and non-English language publications.

Cochrane 2003[70]

The 2003 Cochrane review was conducted using the same 2707 citations obtained from the 2002 report.[15] The citations were rescreened to identify non-English language publications and studies published only as abstracts for inclusion in the Cochrane review. Three additional studies published as abstracts only were included and three studies (seven publications) of jejunoileal bypass were excluded from the Cochrane review (Appendix 16). Eighteen trials reported in 33 publications therefore met the inclusion criteria.

The three additional studies included in the 2003 Cochrane review were:

- RCTs: Agren and Naslund (1989),[73] van Rij (1984)[192] and van Woert *et al*. (1992)[106] (all abstracts).

Cochrane 2005 update[71]

The updated searches in 2005 identified 516 citations, of which 488 were excluded and 28 were retrieved for detailed examination. Thirteen studies were then excluded, and authors of one study were contacted as the eligibility was unclear, but no response was received so this was also excluded (Appendix 16). Fourteen new studies therefore met the inclusion criteria; eight of these were primary studies and six were additional publications of the SOS study included in the first edition of the review.[91–96]

The eight additional primary studies included in the 2005 Cochrane update were:

- RCTs: Davila-Cervantes *et al*. (2002),[111] Lee *et al*. (2004),[124] Lujan *et al*. (2004),[130] Mingrone *et al*. (2002),[119] Morino *et al*. (2003),[110] Sundbom and Gustavsson (2004)[112]
- Cohort studies: Stoeckli *et al*. (2004),[102] von Mach *et al*. (2004).[103]

Current update 2008

The updated searches in 2008 identified 2163 citations, of which 2126 were excluded and 37 were retrieved for detailed examination. Eighteen studies were then excluded (Appendix 16). Nineteen publications therefore met the inclusion criteria; nine of these were new primary studies (three studies each had two publications), two were updates of studies included in previous versions of the review[102,113] and five were additional publications of the SOS study included in all versions of this review.[97–101]

The nine additional primary studies included in this update are:

- RCTs: Angrisani *et al*. (2007),[107] Bessler *et al*. (2007),[118] Dixon *et al*. (2008),[117] Himpens *et al*. (2006),[129] Karamanakos *et al*. (2008),[125] O'Brien *et al*. (2006),[115,116] Olbers *et al*. (2005),[108,109] van Dielen *et al*. (2005),[127,128]
- Cohort study: Buddeberg-Fischer *et al*. (2006).[105]

Studies in original review that were excluded from 2008 update

As a result of the changes in the eligibility criteria for the 2008 update (Chapter 2, Decision problem), a further eight studies (in 14 publications) that were included in previous versions of this review have now been excluded as the surgical procedures assessed (horizontal gastroplasty and vertical gastroplasty without banding) are not in current use (Appendix 16).

A total of 11 studies (in 21 publications) of jejunoileal bypass, horizontal gastroplasty and vertical gastroplasty without banding have therefore been excluded from this update. These are listed in Appendix 16.

In addition, two studies that were included in the 2005 update (Stoeckli *et al.*[102] and von Mach *et al.*[103]) were later identified to be two publications of the same study (this was confirmed by the authors), and have therefore been combined in this update.

Summary of included studies

In summary, a total of 5386 references were identified through the original and updated searches. Twenty-six studies reported in 52 publications met the current inclusion criteria (*Figure 9*).
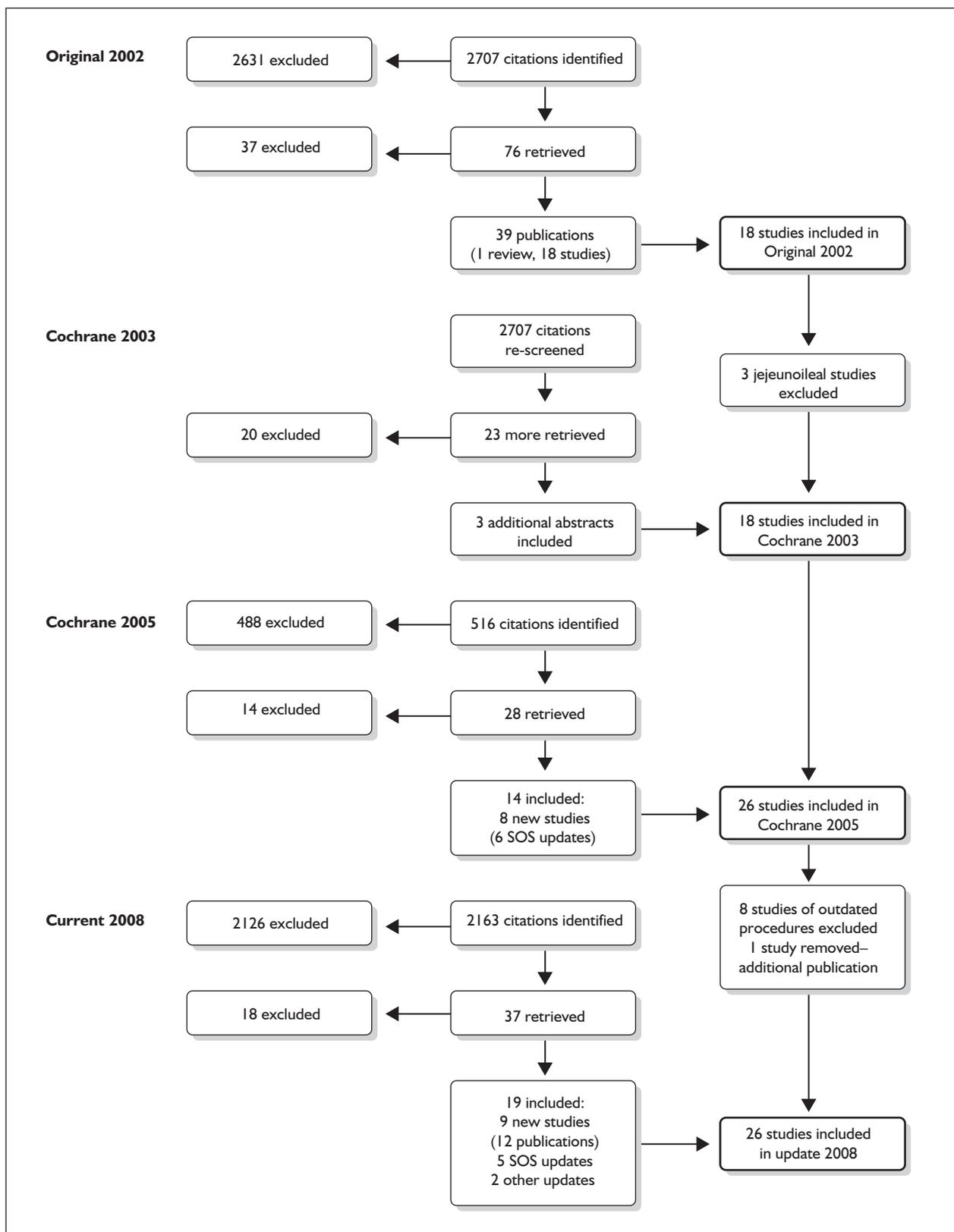
FIGURE 9 *Flow chart of inclusion through the review updates. SOS, Swedish Obese Subjects.*

Appendix 4

Quality assessment

Risk of bias table for included RCTs

Item	Judgement[a]	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 of outcome assessors?[a] (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.)		
Blinding of participants on self-reported outcomes?		
Incomplete outcome data addressed?[a] Weight loss [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 randomised participants), reasons for attrition/exclusions where reported, and any reinclusions in analyses performed by the review authors.]		
Incomplete outcome data addressed?[a] QoL		
Incomplete outcome data addressed?[a] Comorbidity		
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 prespecified in the review's protocol, responses should be provided for each question/item.)		
QoL, quality of life. a 'Yes' indicates low risk of bias, 'No' indicates high risk of bias and 'Unclear' indicates uncertain risk of bias		

Quality assessment criteria for cohort studies

Quality item	Yes/No/Uncertain
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?	

Appendix 18

Updating discounting practice for previous assessment report

Table 74 reports the total costs and QALYs for each morbidly obese (BMI > 40) patient undergoing surgical and non-surgical management, as reported in the previous assessment report. *Table 75* reports the incremental costs for surgical management, with adjustable gastric banding or gastric bypass, compared with non-surgical management. Both surgical procedures are associated with increased total costs and increased QALYs, with ICERs of £8527 for adjustable gastric banding and £6289 for gastric bypass.

The following two tables (*Tables 76* and *Table 77*) report the same analysis, but applying the same discount rate of 3.5% to both costs and QALYs, as is conventional practice in current health technology assessments. This change in discounting practice leads to higher total costs, and reduces the total QALYs as would be expected. However, this change in discounting practice has very little impact on the ICERs, see the final column of *Table 77*.

TABLE 74 *Total net costs and QALYs – discount rates of 6% for costs and 1.5% for QALYs*

	Total Cost (£)	QALYs
Usual care	6964	11.23
SAGB	10,795	11.68
Gastric bypass	9764	11.67
QALYs, quality-adjusted life-years; SAGB, Swedish adjustable gastric band.		

TABLE 75 *Net cost per QALY gained, surgery compared with non-surgical management – discount rates of 6% for costs and 1.5% for QALYs*

Intervention	Comparator	Additional cost (£)	Additional QALYs	Net cost per QALY gained (£)
SAGB	Non-surgical	3831	0.45	8527
Gastric bypass	Non-surgical	2800	0.45	6289
QALYs, quality-adjusted life-years; SAGB, Swedish adjustable gastric band.				

TABLE 76 *Total net costs and QALYs – discount rates of 3.5% for costs and QALYs*

	Total cost (£)	QALYs
Usual care	9044	9.22
SAGB	12,588	9.63
Gastric bypass	11,512	9.64
QALY(s), quality-adjusted life-year(s); SAGB		

TABLE 77 *Net cost per QALY, surgery compared with non-surgical management – discount rates of 3.5% for costs and QALYs*

Intervention	Comparator	Additional cost (£)	Additional QALYs	Net cost per QALY gained (£)
SAGB	Non-surgical	3544	0.41	8553
Gastric bypass	Non-surgical	2468	0.42	5822
QALY(s), quality-adjusted life-year(s); SAGB				

Appendix 19

Caro reparameterisation of Framingham Heart Study accelerated failure time models

Table 78 reports the parameters for the Framingham Heart Study CHD risk equation, as reported by Andersen and colleagues.[168] Andersen and colleagues[168] also outline the method used to derive an individual's risk of a CHD event given their characteristics, in terms of age, sex, systolic blood pressure, smoking status, ratio of total cholesterol to high-density lipoproteins and whether they have developed diabetes.

Table 79 reproduces the steps outlined in the original article by Andersen and colleagues[168] to derive the 10-year predicted probability of a 55-year-old woman, who is a current smoker, with systolic blood pressure of 135 mmHg, and a TC : HDL ratio of 4.79 and who has developed

diabetes. The second column in *Table 78* shows the parameter estimates from the Framingham Heart Study CHD equation, while the third column lists the input values as described in the previous sentence. The final column in *Table 78* lists these input values as they are entered into the risk equation, with log transformations where required (for age, systolic blood pressure and TC : HDL ratio). The first stage in deriving an individual's risk is to multiply the transformed input values by the relevant parameter estimate – the result of this is reported in the row labelled μ in *Table 79*. Following the remaining steps outlined in *Table 79*, gives an estimated 10-year probability of a CHD event of 22%.

TABLE 78 *Parameters for Framingham Heart Study CHD equation from Andersen and colleagues*[168]

	Parameter estimate	Untransformed input value	Transformed input value
θ_0	0.9145		
θ_1	−0.2784		
Constant	15.5305	1	1.0000
Female	28.4441	1	1.0000
ln(Age)	−1.4792	55	4.0073
ln(Age)*Female	−14.4588		4.0073
[ln(Age)]^2*Female	1.8515		16.0587
ln(SBP)	−0.9119	135	4.9053
Smoker	−0.2767	1	1.0000
ln(TC : HDL)	−0.7181	4.79	1.5669
Diabetes	−0.1759	1	1.0000
Diabetes*Female	−0.1999		1.0000

SBP, systolic blood pressure; TC:HDL, total cholesterol to high-density lipoprotein ratio.

TABLE 79 *Steps in calculating an individual's risk of a CHD event*

Calculate example in original paper	
μ	3.58765
$\log(s) = \theta_0 + \theta_1 \mu$	−0.08430
$s = \exp(\theta_0 + \theta_1 \mu)$	0.91915
$u = [\ln(10) - \mu]/s$	−1.39809
10-year predicted probability $\{1 - \exp[-\exp(u)]\}$	0.21891

Alternatively, reparameterising the equation as suggested by Caro and colleagues[169] so that:

$$\lambda = \frac{1}{e^{\mu}}$$

$$\gamma = \frac{1}{e^{\theta_0 + \theta_1 \mu}}$$

allows the use of a more standard Weibull formulation to calculate the hazard in any cycle t:

$$h_t = \lambda^{\gamma} \gamma t^{\gamma - 1}$$

In the above example, this yields an annual risk (assuming annual cycles) from 0.0217 in year 1 to 0.0265 in year 10. Adopting the DEALE method[162] to derive an annual risk from the 10-year risk $[-1/10 * \ln(1 - 0.21891)]$, would yield a constant risk of 0.0247 which would tend to slightly overestimate the risk compared with the method based on the reparameterised FHS equations.

Appendix 20

Variables included in probabilistic sensitivity analyses, distributions and parameters of distributions used

Table 80 and *Table 81* provide details of the included variables.

TABLE 80 *Variables included in probabilistic sensitivity analysis for moderate-to-severely obese (BMI ≥ 30 and < 40) patients with Type 2 diabetes, showing distributions and parameters*

Variable	Distribution	Parameters
Weight loss – surgical	Normal	Mean = 21.1; SD = 1.917
Systolic blood pressure – surgical	Normal	Mean = 6.00; SD = 3.268
TC:HDL – surgical	Normal	Mean = 0.82; SD = 0.347
Weight loss – non-surgical	Normal	Mean = 1.5; SD = 0.986
Systolic blood pressure – non-surgical	Normal	Mean = 1.70; SD = 2.593
TC:HDL – non-surgical	Normal	Mean = 0.14; SD = 0.190
Utility change per unit change in BMI	Uniform	Minimum = 0.0075; SD = 0.0166
Diabetes remission – surgical	Beta	Alpha = 22; Beta = 8
Diabetes remission – non-surgical	Beta	Alpha = 4; Beta = 26
Diabetes heath state	Gamma	Alpha = 4394.9051; Beta = 0.5
Acute AMI	Gamma	Alpha = 3226.4959; Beta = 0.5
Chronic AMI	Gamma	Alpha = 1130.3026; Beta = 0.5
Acute stroke	Gamma	Alpha = 19079.7077; Beta = 0.5
Chronic stroke	Gamma	Alpha = 5129.1832; Beta = 0.5

AMI, acute myocardial infarction; BMI, body mass index; SD, standard deviation; TC:HDL, total cholesterol to high-density lipoprotein ratio.

TABLE 81 *Variables included in probabilistic sensitivity analysis for moderately obese (BMI ≥ 30 and < 35) patients, showing distributions and parameters.*

Variable	Distribution	Parameters
Baseline BMI – surgical	Normal	Mean = 37.7; SD = 0.3827
BMI at 6 months – surgical	Normal	Mean = 28.9; SD = 0.4082
BMI at 12 months – surgical	Normal	Mean = 27; SD = 0.4082
BMI at 18 months – surgical	Normal	Mean = 26.7; SD = 0.4082
BMI at 24 months – surgical	Normal	Mean = 26.4; SD = 0.4082
Systolic blood pressure (% change) – surgical	Beta	Alpha = 4.104; Beta = 33.896
TC:HDL (% change) – surgical	Beta	Alpha = 8.094; Beta = 29.906
Baseline BMI – non-surgical	Normal	Mean = 37.5; SD = 0.4082
BMI at 6 months – non-surgical	Normal	Mean = 28.7; SD = 0.4337
BMI at 12 months – non-surgical	Normal	Mean = 29.9; SD = 0. 4337
BMI at 18 months – non-surgical	Normal	Mean = 30.9; SD = 0. 4337
BMI at 24 months – non-surgical	Normal	Mean = 31.5; SD = 0. 4337
Systolic blood pressure (% change) – non-surgical	Beta	Alpha = 2.160; Beta = 27.840
TC:HDL (% change) – non-surgical	Beta	Alpha = 2.400; Beta = 27.600
Utility change per unit change in BMI	Uniform	Minimum = 0.0075; Maximum = 0.0166
Diabetes remission – surgical	Beta	Alpha = 14; Beta = 1
Diabetes remission – non-surgical	Beta	Alpha = 7; Beta = 8
Diabetes heath state	Gamma	Alpha = 4394.9051; Beta = 0.5
Acute AMI	Gamma	Alpha = 3226.4959; Beta = 0.5
Chronic AMI	Gamma	Alpha = 1130.3026; Beta = 0.5
Acute stroke	Gamma	Alpha = 19079.7077; Beta = 0.5
Chronic stroke	Gamma	Alpha = 5129.1832; Beta = 0.5

AMI, acute myocardial infarction; BMI, body mass index; SD, standard deviation; TC:HDL, total cholesterol to high-density lipoprotein ratio.

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