ClinicalEvidence

Obesity in adults

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ABSTRACT

INTRODUCTION: About one third of the US population and one quarter of the UK population are obese, with increased risks of hypertension, dyslipidaemia, diabetes, cardiovascular disease, osteoarthritis, and some cancers. Fewer than 10% of overweight or obese adults aged 40 to 49 years revert to a normal body weight after 4 years. Nearly 5 million US adults used prescription weight-loss medication between 1996 and 1998, but one quarter of all users were not overweight. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of drug treatments in adults with obesity? What are the effects of bariatric surgery in adults with morbid obesity? We searched: Medline, Embase, The Cochrane Library, and other important databases up to September 2010 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 39 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: bariatric surgery versus medical interventions, biliopancreatic diversion, diethylpropion, gastric bypass, gastric banding, mazindol, orlistat (alone and in combination with sibutramine), phentermine, sibutramine (alone and in combination with orlistat), sleeve gastrectomy, and vertical banded gastroplasty.

QUESTIONS

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What are the effects of bariatric surgery in adults with morbid obesity? . . . 12

INTERVENTIONS

DRUG TREATMENTS IN OBESE ADULTS

Trade off between benefits and harms

Orlistat . . . 3

Phentermine . . . 5

Sibutramine . . . 6

Sibutramine plus orlistat (insufficient evidence to assess combination *v* either intervention alone, however sibutramine is associated with cardiovascular adverse effects) . . . 9

Unknown effectiveness

Diethylpropion . . . 10

Mazindol . . . 11

SURGERY IN MORBIDLY OBESE ADULTS

Likely to be beneficial

Bariatric surgery (more effective than non-surgical treatment for clinically important weight loss in morbidly obese adults, but operative complications common) . . . 12

Gastric bypass . . . 13

Gastric banding . . . 17

Vertical banded gastroplasty . . . 19

Biliopancreatic diversion . . . 20

Unknown effectiveness

Sleeve gastrectomy . . . 21

Covered elsewhere in Clinical Evidence

Obesity in children

Effects of weight loss in preventing cardiovascular disease in the general population: see review on primary prevention of CVD: diet

Key points

- About one third of the US population and one quarter of the UK population are obese, with increased risks of hypertension, dyslipidaemia, diabetes, CVD, osteoarthritis, and some cancers.

  Fewer than 10% of overweight or obese adults aged 40 to 49 years revert to a normal body weight after 4 years.

  Nearly 5 million US adults used prescription weight-loss medication between 1996 and 1998, but one quarter of all users were not overweight.

- Orlistat, phentermine, and sibutramine may promote modest weight loss (an additional 1–7 kg lost) compared with placebo in obese adults having lifestyle interventions, but they can all cause adverse effects.

  Sibutramine may be more effective at promoting weight loss compared with orlistat, although not in obese people with type 2 diabetes or hypertension.

  We don't know whether combining orlistat and sibutramine treatment leads to greater weight loss than with either treatment alone.

  We don't know whether diethylpropion and mazindol are effective at promoting weight loss in people with obesity.

  Orlistat has been associated with GI adverse effects.

Phentermine has been associated with heart and lung problems.

Sibutramine has been associated with cardiac arrhythmias and cardiac arrest. In January 2010, the European Medicines Agency suspended marketing authorisation of sibutramine in the European Union because of the increased risk of non-fatal myocardial infarctions and strokes.

In October 2010, the FDA requested the withdrawal of sibutramine from the US market because of the increased risk of adverse cardiovascular events.

Rimonabant has been associated with an increased risk of psychiatric disorders.

- Bariatric surgery (gastric bypass, vertical banded gastroplasty, biliopancreatic diversion, or gastric banding) may increase weight loss compared with no surgery in people with morbid obesity.
- Compared with each other, we don't know whether gastric bypass, vertical banded gastroplasty, biliopancreatic diversion, or gastric banding is the most effective surgery or the least harmful.

We don't know whether sleeve gastrectomy is effective.

Bariatric surgery may result in loss of >20% of body weight, which may be largely maintained for 10 years.

Operative and postoperative complications are common, and on average 0.28% of people die within 30 days of surgery. Mortality may be as high as 2% in some high-risk populations. However, surgery may reduce long-term mortality compared with no surgery.

DEFINITION

Obesity is a chronic condition characterised by an excess of body fat. It is most often defined by the BMI, a mathematical formula that is highly correlated with body fat. BMI is weight in kilograms divided by height in metres squared (kg/m^2). Worldwide, adults with a BMI of 25 kg/m^2 to 30 kg/m^2 are categorised as overweight, and those with a BMI above 30 kg/m^2 are categorised as obese. [1] [2] Nearly 5 million US adults used prescription weight-loss medication between 1996 and 1998. One quarter of users were not overweight. Inappropriate use of prescription medication is more common among women, white people, and Hispanic people. [3] The National Institutes of Health (NIH) in the US has issued guidelines for obesity treatment, which indicate that all obese adults (BMI >30 kg/m^2), and all adults with a BMI of 27 kg/m^2 or more and with obesity-associated chronic diseases are candidates for drug treatment. [1] Morbidly obese adults (BMI >40 kg/m^2), and all adults with a BMI of 35 kg/m^2 or more and with obesity-associated chronic diseases are candidates for bariatric surgery.

INCIDENCE/ PREVALENCE

Obesity has increased steadily in many countries since 1900. In the UK in 2002, it was estimated that 23% of men and 25% of women were obese. [4] In the past decade alone, the prevalence of obesity in the US has increased from 22.9% between 1988 and 1994, to 34% in 2006. [5] [6]

AETIOLOGY/ RISK FACTORS

Obesity is the result of long-term mismatches in energy balance, where daily energy intake exceeds daily energy expenditure. [7] Energy balance is modulated by a myriad of factors, including metabolic rate, appetite, diet, and physical activity. [8] Although these factors are influenced by genetic traits, the increase in obesity prevalence in the past few decades cannot be explained by changes in the human gene pool, and it is more often attributed to environmental changes that promote excessive food intake and discourage physical activity. [8] [9] Less commonly, obesity may also be induced by drugs (e.g., high-dose glucocorticoids, antipsychotics, antidepressants, oral hypoglycaemic agents, and antiepileptic drugs), or be secondary to various neuroendocrine disorders, such as Cushing's syndrome and PCOS. [10]

PROGNOSIS

Obesity is a risk factor for several chronic diseases, including hypertension, dyslipidaemia, diabetes, CVD, sleep apnoea, osteoarthritis, and some cancers. [1] The relationship between increasing body weight and mortality is curvilinear, where mortality is highest among adults with very low body weight (BMI <18.5 kg/m^2) and among adults with the highest body weight (BMI >35 kg/m^2). [2] Obese adults have more annual admissions to hospitals, more outpatient visits, higher prescription drug costs, and worse health-related quality of life than normal-weight adults. [11] [12] Fewer than 10% of overweight or obese adults aged 40 to 49 years revert to a normal body weight after 4 years. [13]

AIMS OF INTERVENTION

To achieve realistic gradual weight loss, and prevent the morbidity and mortality associated with obesity, without undue adverse effects.

OUTCOMES

Reduction in mortality: we found no RCTs that assessed the primary outcome of reduction in mortality associated with obesity. **Weight loss**: proxy measures assessed in studies included mean weight loss (kg), proportion of people losing 5% or more of baseline body weight, and proportion of people maintaining weight loss. **Adverse effects of treatment.**

METHODS

Clinical Evidence search and appraisal September 2010. The following databases were used to identify studies for this systematic review: Medline 1966 to September 2010, Embase 1980 to September 2010, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials 2010: August (online; 1966 to date of issue). We also searched for retractions of studies included in the review. When editing this review we used The Cochrane Database of Systematic Reviews 2010, Issue 3. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributor for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews of RCTs and of observational studies for surgery in any language. RCTs for drug interventions had to be at least single blinded; for surgical interventions open or blinded studies were acceptable. Studies had to contain 20 or more people. We have excluded RCTs assessing drug treatments with <4 months' follow-up, and RCTs assessing surgical treatments with <1 year's follow-up. We included systematic reviews of RCTs and RCTs where harms of an included intervention were studied applying the same study design criteria for inclusion as we did for benefits. We have also excluded RCTs with >30% loss to follow-up unless they performed an intention-to-treat analysis. However, such RCTs may be included in the meta-analyses of systematic reviews. We did not perform a search for observational studies of bariatric surgery. However, we have included all observational studies of bariatric surgery identified by systematic reviews. In addition we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 24). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the *Clinical Evidence* population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of drug treatments in adults with obesity?

OPTION ORLISTAT

Weight loss

Compared with placebo Orlistat is more effective at increasing weight loss at 6 to 12 months in obese people who are on a low-calorie diet irrespective of having diabetes, hyperlipidaemia, hypertension, or binge eating disorder, but its effects in people with weight gain related to treatment with antipsychotic drugs are less clear (moderate-quality evidence).

Compared with sibutramine Orlistat may be less effective at increasing weight loss in obese people without comorbidities, but we don't know how orlistat and sibutramine compare in people with type 2 diabetes or hypertension (low-quality evidence).

Compared with orlistat plus sibutramine Orlistat seems less effective at increasing weight loss at 6 months in obese people who are also on a reduced-calorie diet (moderate-quality evidence).

Adverse effects

Compared with placebo Orlistat is associated with an increased risk of GI adverse effects such as diarrhoea, flatulence, bloating, and abdominal pain (moderate-quality evidence).

Note

We found no clinically important results from RCTs on orlistat compared with diethylpropion, mazindol, or phentermine in obese people.

For GRADE evaluation of interventions for obesity in adults, see table , p 24 .

Benefits:

Orlistat versus placebo:

We found three systematic reviews (search dates 2003, [14] 2004, [15] and 2006 [16]), which between them identified 23 RCTs (11 of which were identified by all 3 reviews) comparing orlistat versus placebo. We also found 4 additional RCTs, [17] [18] [19] [20] and one subsequent RCT. [21] In all the RCTs identified by the reviews, [14] [15] [16] and in the 4 additional RCTs, [17] [18] [19] [20] people treated with orlistat also followed a low-calorie diet.

The reviews meta-analysed results from RCTs with similar study design and dose of orlistat. The reviews differed slightly in their inclusion criteria for minimum BMI (varied from 25 kg/m^2 to 30 kg/m^2 or >27 kg/m^2 plus 1 or more obesity-related comorbidity), and one review specified a minimum follow-up of 1 year [16] (not set in the other reviews). One review reported subgroup analysis in people with comorbidities. [15] We have therefore reported results from all three reviews.

All three reviews found that orlistat significantly increased weight loss at 1 year compared with placebo, with mean weight loss being similar in all three reviews (mean weight loss ranged from 2.83 kg to 2.89 kg). [14] [15] [16]

The first review found that orlistat significantly increased the mean difference in weight loss at 12 months compared with placebo in people with a minimum BMI of 27 kg/m^2 (22 RCTs; number of people in analysis not reported; mean difference in weight loss: –2.89 kg, 95% CI –3.51 kg to –2.27 kg). [14]

The second review also found that orlistat significantly increased mean weight loss at 12 months compared with placebo in people with a minimum BMI of >25 kg/m^2 (17 RCTs, 10,041 people; WMD in weight loss –2.83 kg, 95% CI –3.54 kg to –2.13 kg). [15] The review also performed separate meta-analyses comparing orlistat versus placebo in people with type 2 diabetes mellitus and other high-risk cardiovascular factors (dyslipidaemia or hypertension). [15] It found that orlistat significantly increased mean weight loss compared with placebo in people with type 2 diabetes mellitus and in people with other high-risk cardiovascular factors (type 2 diabetes: 4 RCTs, 1729 people; WMD in weight loss –2.50 kg, 95% CI –2.97 kg to –2.02 kg; high-risk population: 4 RCTs, 1480 people; WMD in weight loss –2.04 kg, 95% CI –3.21 kg to –0.88 kg). [15]

The third review found that orlistat significantly increased mean weight loss at 12 months compared with placebo in people with a minimum BMI of 30 kg/m^2 or >27 kg/m^2 plus one or more obesity-related comorbidity (14 RCTs, 9457 people; WMD in weight loss –2.87 kg, 95% CI –3.21 kg to –2.53 kg). [16] The review also found that a significantly larger proportion of people lost 5% or more of their initial body weight with orlistat compared with placebo (14 RCTs, 9389 people; 2652/4931 [54%] with orlistat *v* 1468/4458 [33%] with placebo; risk difference 0.21, 95% CI 0.18 to 0.24).

The first additional RCT (90 obese people with type 2 diabetes, hypertension, and metabolic syndrome) found that orlistat (120 mg 3 times daily) significantly increased weight loss at 6 months compared with placebo (mean weight loss –5.6 kg with orlistat *v* –2.6 kg with placebo; P <0.001). [17]

The second additional RCT (384 obese people with dyslipidaemia) found that orlistat (120 mg 3 times daily) significantly increased weight loss at 6 months compared with placebo (mean weight loss –7.4 kg with orlistat *v* –4.9 kg with placebo; P <0.01). [18]

The third additional RCT (1004 obese people with hypertension [614 people], dyslipidaemia [197 people], or type 2 diabetes [193 people]) found that orlistat (120 mg 3 times daily) significantly increased weight loss at 6 months compared with placebo in all populations (mean weight loss in people with type 2 diabetes: –3.9 kg with orlistat *v* –1.3 kg with placebo; hypertension: –5.8 kg with orlistat *v* –1.8 kg with placebo; dyslipidaemia: –5.0 kg with orlistat *v* –2.1 kg with placebo; P <0.0001 for all comparisons). [19]

The fourth additional RCT (89 obese people with binge eating disorder) found that orlistat (120 mg 3 times daily) significantly increased weight loss at 24 weeks compared with placebo (mean % weight lost of initial body weight: 7% with orlistat *v* 2% with placebo; P = 0.0001). [20]

The subsequent RCT (63 obese people having treatment with clozapine or olanzapine for a serious mental condition) found no significant difference between orlistat (120 mg 3 times daily) and placebo in weight loss at 16 weeks (mean change in weight: –1.25 kg with orlistat *v* +0.44 kg with placebo; P = 0.101). [21] Unlike other RCTs of orlistat, people enrolled in the trial, although encouraged to limit their calorie intake, continued on their usual diet. Subgroup analysis based on sex found that, compared with placebo, orlistat significantly increased weight loss at 16 weeks in men (41 men; mean change in weight: –2.36 kg with orlistat *v* +0.62 kg with placebo; P = 0.011), but not in women (22 women; mean change in weight: +1.94 kg with orlistat *v* +0.22 kg with placebo; P = 0.397). The RCT also found no significant difference between groups in the proportion of people losing 5% or more of their initial body weight (5/31 [16%] with orlistat *v* 2/32 [6%] with placebo; P = 0.257).

Orlistat versus sibutramine:

See benefits of sibutramine, p 6 .

Orlistat versus other drugs:
We found one systematic review (search date 1999), which identified no RCTs comparing orlistat versus diethylpropion, mazindol, or phentermine. [22]

Orlistat alone versus orlistat plus sibutramine:
See benefits of sibutramine plus orlistat, p 9 .

Harms:

Orlistat versus placebo:
The first review found that orlistat was associated with a significantly higher risk of GI adverse effects including diarrhoea, flatulence, bloating, abdominal pain, and dyspepsia after 6 to 12 months of treatment compared with placebo (29 RCTs; diarrhoea: OR 54.85, 95% CI 44.88 to 67.48; flatulence: OR 3.72, 95% CI 3.16 to 4.39; bloating, abdominal pain, and dyspepsia: OR 1.55, 95% CI 1.18 to 2.06; absolute numbers not reported for any outcome). [14]

The second review also found that orlistat was associated with a significantly higher risk of GI adverse effects at 1 year compared with placebo (16 RCTs, 9558 people; RR of at least one GI adverse effect: 1.46, 95% CI 1.37 to 1.55; absolute numbers not reported; details of GI adverse effects not described). [15]

The third review found that orlistat was associated with a significantly higher rate of GI adverse effects compared with placebo (14 RCTs, 8938 people; 3805/4684 [81%] with orlistat *v* 2407/4254 [57%] with placebo; risk difference 0.24, 95% CI 0.20 to 0.29). [16] The most commonly reported GI adverse effects reported were fatty/oily stool, faecal urgency, and oily spotting.

The first additional RCT found that orlistat increased the proportion of people with GI adverse events at 4 weeks (36% with orlistat *v* 24% with placebo; absolute numbers not reported; significance not assessed). [17] The second additional RCT gave no information on adverse effects. [18] The third additional RCT found that orlistat was associated with a significantly higher withdrawal rate because of adverse GI effects (mainly defecation difficulties) compared with placebo (10/499 [2.0%] with orlistat *v* 2/505 [0.4%] with placebo; P = 0.01). [19] The fourth additional RCT gave no information on adverse effects. [20]

The subsequent RCT found that a similar proportion of people in the orlistat and placebo groups experienced diarrhoea (11/31 [35%] with orlistat *v* 9/32 [28%] with placebo; significance not assessed). [21]

Orlistat versus sibutramine:
See harms of sibutramine, p 6 .

Orlistat versus other drugs:
We found no RCTs.

Orlistat alone versus orlistat plus sibutramine:
See harms of sibutramine plus orlistat, p 9 .

Comment:
Because of the high rates of GI adverse effects associated with orlistat, it remains unclear whether blinded evaluation of its effects is possible. [23] At the end of a double-blinded 16-week trial, 22/26 (85%) people correctly identified their treatment group.

OPTION PHENTERMINE

Weight loss
Compared with placebo Phentermine seems more effective at increasing weight loss in obese people undertaking additional lifestyle interventions (moderate-quality evidence).

Compared with diethylpropion Phentermine may be more effective at increasing weight loss (low-quality evidence).

Note
Phentermine may be associated with heart and lung problems. We found no direct information from RCTs about weight regain and long-term safety of phentermine in the treatment of adults with obesity. We found no clinically important results from RCTs about phentermine compared with orlistat or sibutramine in obese people.

For GRADE evaluation of interventions for obesity in adults, see table, p 24 .

Benefits:

Phentermine versus placebo:
We found one systematic review (search date 1999; 6 RCTs, 368 people) comparing phentermine 15 mg to 30 mg daily versus placebo in obese adults, with a mean follow-up of 13.2 weeks (range

2–24 weeks). [22] Most of the people treated with phentermine received additional lifestyle interventions. The review found that phentermine produced significantly more weight loss compared with placebo (effect size <0.6 [information presented graphically]; mean difference in weight loss between phentermine and placebo in the 6 RCTs ranged from 0.6 kg to 6.0 kg).

Phentermine versus diethylpropion:
We found one systematic review, which found that phentermine significantly increased weight loss compared with diethylpropion (search date 1999; 1 RCT, 99 people; mean weight loss: –8.3 kg with phentermine *v* –6.3 kg with diethylpropion; effect size: 0.57, CI not reported). [22]

Phentermine versus other drugs:
We found one systematic review, which found no RCTs comparing phentermine versus orlistat, rimonabant, or sibutramine. [22]

Harms:

Phentermine versus placebo/diethylpropion/other drugs:
The systematic review gave no information on adverse effects. [22]

Phentermine given alone has not been associated with valvular heart disease. [24] A European Commission review reported that, although no new safety problems were identified with phentermine, a link between phentermine and heart and lung problems could not be totally excluded. [25]

Comment:

Data regarding the safety and efficacy of phentermine are limited compared with orlistat and sibutramine, and high withdrawal rates have been reported for phentermine. These factors should be considered when making decisions regarding the use of phentermine.

OPTION SIBUTRAMINE

Weight loss
Compared with placebo Sibutramine is more effective at 4 to 12 months at increasing weight loss in obese people who are undertaking dietary interventions with or without exercise, irrespective of co-existing conditions such as diabetes, hypertension, hyperlipidaemia, binge eating disorder, or CAD (moderate-quality evidence).

Compared with orlistat Sibutramine may be more effective at increasing weight loss in obese people without comorbidities, but we don't know how sibutramine and orlistat compare in people with type 2 diabetes or hypertension (low-quality evidence).

Compared with sibutramine plus orlistat We don't know whether sibutramine alone is more effective at increasing weight loss at 6 months in obese people who are also on a reduced-calorie diet or at maintaining weight loss at 16 weeks in obese people with a modified lifestyle who have taken it for 1 year (very low-quality evidence).

Note
Sibutramine has been associated with increases in systolic and diastolic blood pressure, heart rate, and total as well as LDL cholesterol; conversely, it has been associated with modest decreases in triglyceride levels, fasting serum glucose levels, and glycosylated haemoglobin levels, and with modest increases in HDL cholesterol levels. In January 2010, the European Medicines Agency (EMEA) suspended marketing authorisation of sibutramine in the European Union because of the increased risk of non-fatal myocardial infarctions and strokes. In October 2010, the FDA requested the withdrawal of sibutramine from the US market because of the increased risk of adverse cardiovascular events.

For GRADE evaluation of interventions for obesity in adults, see table, p 24 .

Benefits:

Sibutramine versus placebo:
We found two systematic reviews, [26] [16] two additional RCTs, [27] [28] and two subsequent RCTs comparing sibutramine versus placebo. [29] [30] The two reviews, which between them identified 34 RCTs, differed in their inclusion criteria, and so included different RCTs in their meta-analysis. We report both reviews here. Most of the people treated with sibutramine received additional dietary interventions, and many also received an exercise intervention. The first review suggested that weight loss with sibutramine is associated with both positive and negative changes in cardiovascular and metabolic risk factors. [26]

The first review (search date 2002; 29 RCTs [number of people not reported] in people with BMI 25–40 kg/m^2, some with diabetes, hypertension, hyperlipidaemia, or binge eating disorder) included unpublished RCTs (authors of the review contacted key researchers in the field and pharmaceutical companies), and RCTs with a minimum follow-up of 8 weeks. [26] The review meta-analysed data in three groups based on follow-up of 8 to 12 weeks, 16 to 24 weeks, and 44 to 54 weeks. For drug interventions, our minimum length of follow-up for reporting is 4 months, and so we report only meta-analysis of data at 16 weeks or more of follow-up. All the meta-analyses found that sibutramine

significantly increased weight loss compared with placebo. Trials of 16 to 24 weeks' duration, all comparing sibutramine 10 mg to 15 mg daily versus placebo, were meta-analysed in three subgroups because of significant heterogeneity among the trials in methods of analysis (statistically heterogeneous; P <0.001). All the meta-analyses found that sibutramine significantly increased weight loss compared with placebo (4 RCTs [484 people] that used last-observation-carried-forward analysis and had >70% follow-up: WMD –3.43 kg, 95% CI –4.50 kg to –2.36 kg; 5 RCTs [473 people] that assessed completers: –6.03 kg, 95% CI –7.36 kg to –4.70 kg; 3 RCTs [222 people] with follow-up of <70%: –5.06 kg, 95% CI –6.16 kg to –3.96 kg); people who completed the trial had the greatest weight loss. The review also found that sibutramine 10 mg to 15 mg daily significantly increased weight loss at 45 to 54 weeks compared with placebo (5 RCTs, 2188 people; WMD –4.45 kg, 95% CI –5.29 kg to –3.62 kg). The review found similar rates of weight loss in trials that specifically recruited obese adults with type 2 diabetes mellitus, hypertension, or hyperlipidaemia, and in trials in obese adults who did not have comorbidities (data not reported in review). [26]

The second review (search date 2006; 10 RCTs, 2348 people with BMI 30 kg/m^2 or >27 kg/m^2 plus 1 or more obesity-related comorbidity) included only published RCTs with a minimum length of follow-up of 1 year. [16] The review found that sibutramine significantly increased mean weight loss at 12 months compared with placebo (10 RCTs, 2348 people; WMD weight loss –4.16 kg, 95% CI –4.73 kg to –3.59 kg). The review also found that a significantly larger proportion of people lost 5% or more of their initial body weight with sibutramine compared with placebo (7 RCTs, 1464 people; 443/808 [57%] with sibutramine *v* 174/656 [25%] with placebo; risk difference 0.32, 95% CI 0.27 to 0.37). The review combined data on weight loss from RCTs separately assessing weight loss and weight maintenance in the same analysis.

The first additional RCT (48 obese adults with type 2 diabetes) compared sibutramine 15 mg daily versus placebo for 6 months. [27] It found that sibutramine significantly increased mean weight loss at 6 months compared with placebo (–2.4 kg with sibutramine *v* –0.7 kg with placebo; P <0.05). The second additional RCT (80 obese adults with CAD) compared sibutramine 10 mg daily versus placebo for 4 months. [28] It found that sibutramine significantly increased percentage weight reduction from initial body weight at 4 months compared with placebo (11% with sibutramine *v* 2% with placebo; P <0.001).

The first subsequent RCT (138 people with BMI 30 kg/m^2 or more and who had type 2 diabetes mellitus and inadequate glycaemic control on a sulphonylurea or metformin) compared sibutramine 10 mg daily versus placebo for 6 months. [29] It found that sibutramine significantly increased weight loss at 6 months compared with placebo (change in body weight from baseline: from 102 kg to 96 kg with sibutramine *v* from 101 kg to 100 kg with placebo; P <0.05). Before randomisation to sibutramine or placebo, all people enrolled completed a 3-month run-in period in which they took a fixed dose of pioglitazone, and started a low-calorie diet (about 600 kcal daily deficit). Treatment with pioglitazone continued for the duration of the study. The RCT reported no large changes in body weight in the run-in phase in either group. [29] The second subsequent RCT (171 people with BMI of 27–45 kg/m^2 and hypertension) compared sibutramine 15 mg daily versus placebo over 16 weeks. [30] It found that sibutramine significantly increased mean weight loss at 16 weeks compared with placebo (–5.7 kg with sibutramine *v* –1.5 kg with placebo; P <0.0001). The RCT also found that a significantly larger proportion of people lost 5% or more of their initial body weight with sibutramine compared with placebo (54.7% with sibutramine *v* 14.5% with placebo; absolute numbers not reported; P <0.0001). General dietary and exercise advice was given to people enrolled in the RCT. [30]

Sibutramine versus orlistat:

We found one systematic review (search date 2007; 8 RCTs, 885 people, some with diabetes or hypertension) comparing sibutramine versus orlistat. [31] The review found that sibutramine (10 mg daily in 6 RCTs, 15 mg daily in 1 RCT, and 20 mg daily in 1 RCT) significantly increased weight loss compared with orlistat (120 mg 3 times daily) at 3 to 12 months (median duration 7 months; 7 RCTs, 795 people; WMD in weight loss –2.2 kg, 95% CI –3.9 kg to –0.5 kg). However, the review reported significant heterogeneity among the RCTs (statistically heterogeneous: P <0.001). Two of the RCTs included in the meta-analysis were subgroup analyses of people with type 2 diabetes or hypertension. When meta-analysing results in people with and without comorbidities separately, results of both meta-analyses were statistically homogeneous. Analysis of those RCTs not specifically assessing people with type 2 diabetes or hypertension found the difference in weight loss at 3 to 8.8 months between sibutramine and orlistat to be significant in favour of sibutramine (5 RCTs, 478 people; WMD in weight loss –3.4 kg, 95% CI –4.6 kg to –2.3 kg). However, in people with type 2 diabetes or hypertension, the review found no significant difference in weight loss at 12 months between sibutramine and orlistat (2 RCTs, 253 people; WMD in weight loss +0.4 kg, 95% CI –0.6 kg to +1.4 kg).

Sibutramine versus diethylpropion, mazindol, or phentermine:
We found one systematic review (search date 1999), which identified no RCTs comparing sibutramine versus diethylpropion, mazindol, or phentermine. [22]

Sibutramine plus orlistat:
See benefits of sibutramine plus orlistat, p 9 .

Harms:

Sibutramine was temporarily suspended from the market in Italy in March 2002 in response to 50 reported adverse reactions, including 7 severe adverse reactions (tachycardia, hypertension, and arrhythmia) and two deaths resulting from cardiac arrest. The Central European Committee for Proprietary Medicinal Products completed a review of sibutramine in June 2002, and concluded that the risk–benefit profile of sibutramine remained in favour of benefit; it therefore lifted the suspension in August 2002. [32] However, sibutramine has subsequently been evaluated by the European Medicines Agency (EMEA). The Agency's Committee for Medicinal Products for Human Use concluded that the risks are greater than the benefits and recommended suspending marketing of sibutramine in the European Union in January 2010. Additionally, since the search date of this review, the FDA has concluded that the risk for an adverse cardiovascular event outweighs the modest weight loss observed with sibutramine and has requested the withdrawal of this drug product from the US market (see drug safety alert below for further information).

Sibutramine versus placebo:
We found no evidence about adverse effects after more than 1 year of treatment.

General adverse effects:
The first review found that sibutramine was associated with increased total and LDL cholesterol levels at 16 to 24 weeks compared with placebo (increase in total cholesterol [data reported are mean difference of sibutramine minus placebo]: –1.9 mg/dL to +1.8 mg/dL; increase in LDL cholesterol: 0.6 mg/dL to 2.6 mg/dL); however, no difference from baseline levels was noted at 44 to 54 weeks. [26]

The second review reported that insomnia, nausea, dry mouth, and constipation were more common in people receiving sibutramine, occurring at frequency rates of 7% to 20% (absolute numbers not reported; significance not assessed). [16]

The first additional RCT found no significant difference between sibutramine and placebo in serum triglycerides, total cholesterol, LDL cholesterol, or HDL cholesterol (triglycerides: 1.9 mmol/L with sibutramine *v* 2.6 mmol/L with placebo; total cholesterol: 4.9 mmol/L in each group; LDL cholesterol: 3.0 mmol/L with sibutramine *v* 2.8 mmol/L with placebo; HDL cholesterol: 1.1 mmol/L with sibutramine *v* 1.0 mmol/L with placebo; all comparisons reported as not significant; P value not reported for any outcome). [27]

Cardiovascular adverse effects:
The first review found that sibutramine increased systolic blood pressure and diastolic blood pressure compared with placebo (mean difference in systolic blood pressure [data reported are mean difference of sibutramine minus placebo]: range from –1.6 mmHg to +5.6 mmHg at 16–24 weeks in several RCTs, +4.6 mmHg at 44–54 weeks; mean difference in diastolic blood pressure: +1.6 mmHg at 8–12 weeks, –0.8 mmHg to +1.7 mmHg at 16–24 weeks, and +2.8 mmHg at 44–54 weeks in several RCTs). [26] The review found significant heterogeneity (statistically heterogeneous; P <0.001) among RCTs assessing blood pressure and reported change in systolic and diastolic blood pressures across RCTs. It also found that sibutramine significantly increased heart rate compared with placebo (increase in heart rate 0.75–5.9 bpm at 16–24 weeks, and 5.9 bpm at 44–54 weeks). [26]

The second review also found that, compared with placebo, sibutramine was associated with significant increases in systolic (7 RCTs, 1906 people; WMD 1.69 mmHg, 95% CI 0.11 mmHg to 3.28 mmHg) and diastolic blood pressure at 12 months (7 RCTs, 1906 people; WMD 2.42 mmHg, 95% CI 1.51 mmHg to 3.32 mmHg). [16] Sibutramine was also associated with significant increase in heart rate at 12 months compared with placebo (7 RCTs, 1658 people; WMD in heart rate 4.53 bpm, 95% CI 3.49 bpm to 5.57 bpm).

The first additional RCT found no significant difference between sibutramine and placebo in heart rate, systolic blood pressure, or diastolic blood pressure (heart rate: 74 bpm in both groups; systolic blood pressure: 135 mmHg with sibutramine *v* 133 mmHg with placebo; diastolic blood pressure: 87 mmHg with sibutramine *v* 88 mmHg with placebo; all comparisons reported as not significant; P value not reported for any outcome). [27] The second additional RCT reported no differences in mean systolic or diastolic blood pressure, or in heart rate during the 4-month follow-up between the sibutramine and placebo groups (absolute numbers not reported; significance not assessed). [28]

The first subsequent RCT found that the change in systolic blood pressure and diastolic blood pressure at 6 months was similar with sibutramine and placebo (change from baseline; systolic blood pressure: from 135.6 mmHg to 133.2 mmHg with sibutramine *v* from 136.1 mmHg to 134.4 mmHg with placebo; diastolic blood pressure: from 86.9 mmHg to 84.0 mmHg with sibutramine *v* from 85.9 mmHg to 84.2 mmHg with placebo; significance not assessed for either outcome). [29] The RCT gave no information on other adverse effects. The second subsequent RCT found no significant difference between sibutramine and placebo in change in systolic or diastolic blood pressure at 16 weeks (mean change from baseline; systolic blood pressure: –5.9 mmHg with sibutramine *v* –4.8 mmHg with placebo; P = 0.5494; diastolic blood pressure: –0.7 mmHg with sibutramine *v* –2.3 mmHg with placebo; P = 0.1785). [30] However, the RCT found that sibutramine was associated with a significant increase in 24-hour diastolic blood pressure at 16 weeks compared with placebo (mean change from baseline: +2.1 mmHg with sibutramine *v* –0.3 mmHg with placebo; P = 0.0403), but there was no significant difference between groups in 24-hour systolic blood pressure (–0.3 mmHg with sibutramine *v* –0.9 mmHg with placebo; P = 0.6939). Similarly, the RCT found that sibutramine was associated with a significant increase in heart rate at 16 weeks compared with placebo (mean change from baseline heart rate: +4.5 bpm with sibutramine *v* –1.4 bpm with placebo; P <0.0001). [30]

We found two further RCTs assessing the effects of sibutramine on heart-valve function. [33] [34] Both of these RCTs may have been too small to detect clinically important adverse effects. The first RCT (210 obese people) compared sibutramine versus placebo for 12 months. [34] It found no significant difference in the incidence of valvular disease between sibutramine and placebo (3/133 [2.3%] with sibutramine 15–20 mg/day *v* 2/77 [2.6%] with placebo; OR 0.87, 90% CI 0.19 to 3.97). The trial gave no information on efficacy. The second RCT (184 obese people) compared sibutramine 10 mg or 20 mg daily versus placebo. [33] It reported no change in valvular appearance on echocardiogram in any group (no statistical comparisons between or within groups reported). [33]

Sibutramine versus orlistat:
The systematic review gave no information on treatment-related adverse effects. [31] The review found no significant difference between sibutramine and orlistat in rate of withdrawal (4 RCTs, 369 people; 9/184 [5%] with sibutramine *v* 16/185 [9%] with orlistat; RR 0.6, 95% CI 0.3 to 1.4). However, the review noted that three of four RCTs included in the meta-analysis reported a lower risk of withdrawal with sibutramine compared with orlistat.

Sibutramine versus diethylpropion, mazindol, or phentermine:
We found no RCTs comparing sibutramine versus other drugs.

Sibutramine plus orlistat:
See harms of sibutramine plus orlistat, p 9 .
Drug safety alert:
The European Medicines Agency (EMEA) has suspended marketing of sibutramine because of the increased risk of non-fatal myocardial infarctions and strokes (www.ema.europa.eu). The FDA has requested the withdrawal of sibutramine from the US market (www.fda.gov).

Comment:

Clinical guide:
Sibutramine has been associated with increases in systolic and diastolic blood pressure, heart rate, and total as well as LDL cholesterol; conversely, it has been associated with modest decreases in triglyceride levels, fasting serum glucose levels, glycosylated haemoglobin levels, and modest increases in HDL cholesterol levels. [16] [26]

OPTION SIBUTRAMINE PLUS ORLISTAT

Weight loss
Compared with orlistat alone Sibutramine plus orlistat seems more effective at increasing weight loss at 6 months in obese people who are also on a reduced-calorie diet (moderate-quality evidence).

Compared with sibutramine alone We don't know whether sibutramine plus orlistat is more effective at increasing weight loss at 6 months in obese people who are also on a reduced-calorie diet or at maintaining weight loss at 16 weeks in obese people with a modified lifestyle who have taken it for 1 year (very low-quality evidence).

Note
Sibutramine has been associated with increases in systolic and diastolic blood pressure, heart rate, and total as well as LDL cholesterol; conversely, it has been associated with modest decreases in triglyceride levels, fasting serum glucose levels, and glycosylated haemoglobin levels, and with modest increases in HDL cholesterol levels. In January 2010, the European Medicines Agency (EMEA) suspended marketing authorisation of sibutramine in the European Union because of the increased risk of non-fatal myocardial infarctions and strokes. In October 2010, the FDA requested the withdrawal of sibutramine from the US market because of the increased risk of adverse cardiovascular

events We found no direct information from RCTs about whether sibutramine plus orlistat is better than no active treatment.

For GRADE evaluation of interventions for obesity in adults, **see table, p 24 .**

Benefits:

Sibutramine plus orlistat versus placebo:
We found no systematic review or RCTs.

Sibutramine plus orlistat versus orlistat alone:
We found one RCT comparing three treatments for weight loss for 6 months: sibutramine (15 mg daily) plus orlistat (120 mg 3 times daily), sibutramine alone (15 mg daily), and orlistat alone (120 mg 3 times daily). [35] All people enrolled also followed a reduced-calorie diet. It found that sibutramine plus orlistat significantly increased mean weight loss compared with orlistat alone at 6 months (3-arm RCT; 89 obese women; mean weight loss: 10.8 kg with sibutramine plus orlistat *v* 5.5 kg with orlistat alone; P = 0.002). [35]

Sibutramine plus orlistat versus sibutramine alone:
We found two RCTs, one assessing weight loss [35] and the other assessing weight-loss maintenance. [23] The first RCT compared three treatments for weight loss for 6 months: sibutramine (15 mg daily) plus orlistat (120 mg 3 times daily), sibutramine alone (15 mg daily), and orlistat alone (120 mg 3 times daily). [35] All people enrolled also followed a reduced-calorie diet. The RCT found no significant difference between sibutramine plus orlistat and sibutramine alone in weight loss at 6 months (3-arm RCT; 89 obese women; mean weight loss: 10.8 kg with sibutramine plus orlistat *v* 10.1 kg with sibutramine alone; P = 0.35). The second RCT compared sibutramine (10–15 mg daily) plus orlistat (120 mg 3 times daily) versus sibutramine plus placebo for weight-loss maintenance. [23] It found no significant difference between treatments in mean body weight after 16 weeks (34 women who had completed 1 year of sibutramine alone plus lifestyle modification; mean change in body weight: +0.1 kg with sibutramine plus orlistat *v* +0.5 kg with sibutramine plus placebo; difference reported as not significant; P value not reported). Considering the small study size and the large withdrawal rate (only 76% of the women completed the study), these results should be interpreted with caution.

Sibutramine plus orlistat versus other drugs:
We found no RCTs.

Harms:

Sibutramine plus orlistat versus placebo:
We found no RCTs.

Sibutramine plus orlistat versus orlistat alone:
The RCT gave no information on adverse effects. [35]

Sibutramine plus orlistat versus sibutramine alone:
The first RCT gave no information on adverse effects. [35] The second RCT found that sibutramine plus orlistat significantly increased GI adverse effects (soft stools, bowel movements, oily evacuation, and faecal urge) compared with sibutramine plus placebo at 68 weeks (soft stools: 50% with sibutramine plus orlistat *v* 9% with sibutramine plus placebo; P = 0.04; increased frequency of bowel movements: 50% with sibutramine plus orlistat *v* 9% with sibutramine plus placebo; P = 0.04; oily evacuation: 43% with sibutramine plus orlistat *v* 0% with sibutramine plus placebo; P = 0.02; faecal urgency: 43% with sibutramine plus orlistat *v* 9% with sibutramine plus placebo; P = 0.02). [23]

For further information on adverse effects associated with sibutramine, see harms of sibutramine alone, p 6 .

Sibutramine plus orlistat versus other drugs:
We found no RCTs.
Drug safety alert:
The European Medicines Agency (EMEA) has suspended marketing of sibutramine because of the increased risk of non-fatal myocardial infarctions and strokes (www.ema.europa.eu). The FDA has requested the withdrawal of sibutramine from the US market (www.fda.gov).

Comment: None.

OPTION DIETHYLPROPION

Weight loss
Compared with placebo Diethylpropion may be more effective at 6 months at increasing weight loss in obese adults who are on a hypocaloric diet (low-quality evidence).

Compared with phentermine Diethylpropion may be less effective at increasing weight loss (low-quality evidence).

Adverse effects
Compared with placebo Diethylpropion may be associated with an increased risk of dry mouth and insomnia at the beginning of therapy in obese adults who are on a hypocaloric diet (low-quality evidence).

For GRADE evaluation of interventions for obesity in adults, see table , p 24 .

Benefits:

Diethylpropion versus placebo:
We found one RCT (69 adults with a BMI of 30–45 kg/m^2) comparing diethylpropion versus placebo for 6 months (data from the phase 2 open-label extension in which all people who completed phase 1 of the trial then received diethylpropion for an additional 6 months are not included in this review). [36] All participants were instructed to follow a hypocaloric diet and counselled to carry through at least 150 minutes of physical activity a week. The RCT found that diethylpropion (50 mg twice daily) significantly increased mean weight loss at 6 months compared with placebo (–9.3 kg with diethylpropion *v* –3.1 kg with placebo; P <0.0001). The RCT also found that a significantly larger proportion of people lost 5% or more of their initial body weight with diethylpropion compared with placebo at 6 months (68% with diethylpropion *v* 25% with placebo; P = 0.0005, absolute numbers not reported). Additionally, the RCT found that the proportion of people achieving a 10% or greater weight loss was significantly higher with diethylpropion compared with placebo at 6 months (51% with diethylpropion *v* 3% with placebo; P <0.0001; absolute numbers not reported). [36]

Diethylpropion versus phentermine:
See benefits of phentermine, p 5 .

Diethylpropion versus orlistat:
See benefits of orlistat, p 3 .

Diethylpropion versus sibutramine:
See benefits of sibutramine, p 6 .

Harms:

Diethylpropion versus placebo:
The RCT found that diethylpropion was associated with an increased rate of dry mouth and insomnia during the first 3 months of therapy (dry mouth: 69% with diethylpropion *v* 41% with placebo; P = 0.02; insomnia: 53% with diethylpropion *v* 22% with placebo; P = 0.009; absolute numbers not reported). [36] After 3 months, no significant difference in reported adverse events were observed between the two groups. [36]

Diethylpropion versus phentermine:
See harms of phentermine, p 5 .

Diethylpropion versus orlistat:
See harms of orlistat, p 3 .

Diethylpropion versus sibutramine:
See harms of sibutramine, p 6 .

Comment: None.

OPTION MAZINDOL

We found no direct information from RCTs about whether mazindol is better than no active treatment or other drugs in the treatment of adults with obesity.

For GRADE evaluation of interventions for obesity in adults, see table , p 24 .

Benefits:

Mazindol versus placebo:
We found no systematic review or RCTs.

Mazindol versus orlistat:
See benefits of orlistat, p 3 .

Mazindol versus sibutramine:
See benefits of sibutramine, p 6 .

Harms:

Mazindol versus placebo:
We found no RCTs.

Mazindol versus orlistat:
See harms of orlistat, p 3 .

Mazindol versus sibutramine:
See harms of sibutramine, p 6 .

Comment: None.

QUESTION What are the effects of bariatric surgery in adults with morbid obesity?

OPTION BARIATRIC SURGERY VERSUS NON-SURGICAL TREATMENT

Weight loss
Compared with non-surgical treatment Bariatric surgery (gastric banding, gastric bypass, vertical banded gastroplasty, and biliopancreatic diversion) may be more effective than non-surgical treatments (predominantly lifestyle modification to reduce calorie intake and increase exercise) at increasing weight loss and percentage of initial weight lost at 1 to 10 years (low-quality evidence).

Note
We found no direct information from RCTs on the effects of sleeve gastrectomy compared with non-surgical treatment.

For GRADE evaluation of interventions for obesity in adults, see table, p 24 .

Benefits:

We found one systematic review (search date 2008), [37] which identified two RCTs and three cohort studies in people with morbid obesity. The RCTs and cohorts compared various bariatric surgical techniques (gastric banding, gastric bypass, vertical banded gastroplasty, and biliopancreatic diversion) versus non-surgical treatment. Types of surgery differed between RCTs and cohort studies, and some studies combined data for different surgical techniques. There was also considerable variation in the non-surgical treatment given.

The first RCT (60 people; BMI 30–40 kg/m^2 [mean BMI of >37.0 kg/m^2 in both groups]; all with type 2 diabetes) identified by the review compared laparoscopic adjustable gastric banding versus non-surgical treatment (lifestyle modification programme structured to reduce calorie intake and increase exercise; drug treatments also allowed). [37] At 2 years, the review found that, compared with non-surgical treatment, laparoscopic adjustable gastric banding significantly increased mean weight loss and percentage of initial weight lost (mean weight loss: –21.1 kg with laparoscopic adjustable gastric banding *v* –1.5 kg with non-surgical treatment; difference –19.6 kg, 95% CI –23.8 kg to –15.2 kg; P <0.001; percentage of initial weight lost: 20.0% with laparoscopic adjustable gastric banding *v* 1.4% with non-surgical treatment; P <0.001).

The second RCT (79 people; BMI >40 kg/m^2) identified by the review compared biliopancreatic diversion versus non-surgical treatment (calorie-controlled diet; modified every 6 months). The review found that weight loss at 1 year was greater with biliopancreatic diversion in men and women compared with calorie-controlled diet (change in weight from baseline; women: from 125.3 kg to 90.2 kg with biliopancreatic diversion *v* from 121.6 kg to 114.5 kg with calorie-controlled diet; men: from 151.8 kg to 99.7 kg with biliopancreatic diversion *v* from 147.3 kg to 138.2 kg with calorie-controlled diet; significance not assessed). [37]

The first cohort study (4047 people: mean BMI of 42.4 kg/m^2 in surgical group and 40.1 kg/m^2 in non-surgical group) identified by the review was a multicentre, prospective cohort study comparing bariatric surgery versus usual care. [37] Eligible people self-selected either bariatric surgery or non-surgical (usual) care. Each person who selected surgical treatment was matched on 18 clinical variables with a person from the usual care group. Each surgeon determined the surgical procedure offered: vertical banded gastroplasty (>70%), gastric bypass (6%), or gastric banding (23%). Usual care was according to local practice and usually did not include pharmacotherapy. The study found that bariatric surgery significantly increased weight loss at 2 years compared with usual care (3505 people assessed; mean change in body weight: –23.4% with surgery *v* +0.1% with usual care; P <0.001). Long-term follow-up found that the difference in weight loss between groups remained significant at 10 years (1703 people assessed; mean change in body weight: –16.1% with surgery *v* +1.6% with usual care; P <0.001). There was variation in the mean percentage of weight lost at 10 years with type of bariatric procedure performed (mean weight loss [number of people assessed]: –25.0% with gastric bypass [58/265 people] *v* –16.0% with vertical banded gastroplasty [746/1369 people] *v* –14.0% with gastric banding [237/376 people]; significance not assessed).

The second cohort study (93 people [mean BMI >40 kg/m^2 in both groups], with 63 people in the surgery group and 30 people in the non-surgical treatment group) identified by the review compared laparoscopic adjustable gastric banding or laparoscopic gastric bypass versus non-surgical treatment. [37] The review found that mean excess-weight loss at a mean follow-up of 3.2 years was significantly greater with surgery compared with non-surgical treatment (42.2% with surgery *v* 11.5% with non-surgical treatment; P <0.001).

The third cohort study (20 people; mean BMI >40 kg/m^2 in both groups) identified by the review compared laparoscopic adjustable gastric banding versus gastric bypass versus non-surgical treatment. [37] The review found that mean BMI at 2 years was significantly lower with both surgeries compared with non-surgical treatment (32.9 kg/m^2 with gastric bypass *v* 33.2 kg/m^2 with laparoscopic adjustable gastric banding *v* 41.0 kg/m^2 with non-surgical treatment; P <0.001 for both comparisons of surgery versus non-surgical treatment).

Harms:

The RCT comparing laparoscopic adjustable gastric banding versus non-surgical treatment reported no deaths in either arm. [37] The second RCT gave no information on adverse effects.

The first cohort study reported 5 postoperative deaths in 2010 people (0.25%): three deaths owing to leakage; one owing to a technical mistake during laparoscopic surgery; and one owing to postoperative myocardial infarction. [37] It also reported that 151/1164 (13%) of people experienced postoperative complications (including bleeding 0.9%; thromboembolism 0.8%; wound complications 1.8%; deep infections 2.1%; pulmonary complications 6.1%; and other complications 4.8%; absolute numbers not reported), and that 26/1164 (2%) people required re-operation.

The second cohort study gave information on re-operation rate only. It reported that 7/56 (13%) of people who had laparoscopic gastric banding required re-operation. The cohort study also reported that 9/37 (24%) people in the non-surgical group had gastric bypass. [37]

The third cohort study gave no information on adverse effects. [37]

Comment:

Clinical guide:
Evidence regarding the efficacy and safety of bariatric surgical procedures comes from studies of mostly young, white women. [37] Therefore, these results may not be generalisable to other populations.

OPTION GASTRIC BYPASS

Weight loss

Compared with vertical banded gastroplasty Gastric bypass seems more effective at increasing weight loss at 1 to 3 years (moderate-quality evidence).

Compared with gastric banding Gastric bypass is more effective at increasing weight loss at 4 to 5 years (high-quality evidence).

Compared with biliopancreatic diversion Gastric bypass seems less effective at increasing excess-weight loss at 1 year (moderate-quality evidence).

Compared with sleeve gastrectomy Gastric bypass seems less effective at increasing excess-weight loss at 1 year compared with sleeve gastrectomy (moderate-quality evidence).

Proximal compared with distal gastric bypass Proximal and distal gastric bypass seem equally effective at increasing weight loss at 1 to 3 years (moderate-quality evidence).

Open gastric bypass compared with laparoscopic gastric bypass We don't know whether open gastric bypass is more effective than laparoscopic gastric bypass at increasing weight loss (low-quality evidence).

Note

Gastric bypass is associated with nutritional and electrolyte abnormalities, GI symptoms, and surgical complications. There is a small risk of perioperative death with gastric bypass, but postoperative complications are common and may require re-operation. Laparoscopic gastric bypass reduces hospital stay compared with open gastric bypass.

For GRADE evaluation of interventions for obesity in adults, **see table, p 24 .**

Benefits:

We found one systematic review (search date 2003) reporting that gastric bypass resulted in a mean weight loss of 43.5 kg (95% CI 41.2 kg to 43.5 kg; 32 RCTs, non-randomised controlled trials, and case series; 2937 people) at 12-month follow-up, and 41.5 kg (95% CI 37.4 kg to 45.6 kg; 21

RCTs, non-randomised controlled trials, and case series; 1281 people) at 36-month follow-up and beyond. [38]

Gastric bypass versus vertical banded gastroplasty:
We found one systematic review (search date 2008; 7 RCTs, 435 people), [37] which identified 6 RCTs comparing gastric bypass versus vertical banded gastroplasty, and one RCT comparing three interventions. The systematic review did not pool data and so we report data from the individual RCTs. Two of the RCTs were reported as abstracts only and are not discussed further. Data reported are as reported in the review. [37]

The first RCT (42 adults with BMI 40 kg/m^2 or more) found that gastric bypass significantly increased weight loss at 12 months compared with vertical banded gastroplasty (% excess-weight lost: 78% with gastric bypass *v* 52% with vertical banded gastroplasty; P <0.05; data estimated by review from figure). [37]

The second RCT (40 adults who were >44 kg overweight) also found that gastric bypass significantly increased weight loss compared with vertical banded gastroplasty at 12 months, 2 years, and 3 years (% of excess-weight lost: 12 months: 68% with gastric bypass *v* 43% with vertical banded gastroplasty; P <0.001; 2 years: 66% with gastric bypass *v* 39% with vertical banded gastroplasty; P <0.001; 3 years: 62% with gastric bypass *v* 37% with vertical banded gastroplasty; P <0.001; data for 2 and 3 years estimated by review from a figure). [37]

The third RCT (80 people with morbid obesity) found that laparoscopic gastric bypass significantly increased weight loss compared with laparoscopic vertical banded gastroplasty at 1 and 2 years' follow-up (% excess-weight lost: at 1 year: 63% with gastric bypass *v* 55% with vertical banded gastroplasty; at 2 years: 71% with gastric bypass *v* 53% with vertical banded gastroplasty; reported as significant; P values not reported). [37]

The fourth RCT (83 people with morbid obesity) also found that laparoscopic gastric bypass significantly increased weight loss compared with laparoscopic vertical banded gastroplasty at 1 and 2 years' follow-up (% excess-weight lost; at 1 year: 78% with gastric bypass *v* 63% with vertical banded gastroplasty; P = 0.009; at 2 years: 84% with gastric bypass *v* 60% with vertical banded gastroplasty; P <0.001). [37]

The fifth RCT (106 people; mean BMI of >48 kg/m^2 in both groups) found no significant difference in success rate (defined as proportion of people with BMI of <35 kg/m^2 or <50% excess weight) between the two procedures at 3 years and 5 to 6 years (at 3 years: 30/52 [58%] with gastric bypass *v* 21/54 [39%] with vertical banded gastroplasty; P = 0.08; at 5–6 years: 16/52 [34%] with gastric bypass *v* 9/54 [16%] with vertical banded gastroplasty; P = 0.112). [37]

Gastric bypass versus gastric banding:
We found one systematic review (search date 2008), which identified one RCT, [37] and one subsequent RCT. [39] The RCT included in the review (51 adults with BMI 35–50 kg/m^2 [mean BMI >43.0 kg/m^2 in both groups]) compared laparoscopic gastric bypass versus laparoscopic adjustable gastric banding. It found that gastric bypass significantly increased excess-weight loss at 5 years (% excess-weight lost: 66.6% with gastric bypass *v* 47.5% with gastric banding; P <0.001). [37] The subsequent RCT (197 people with BMI 40–60 kg/m^2 [mean BMI: 47.5 kg/m^2 in the gastric bypass group *v* 45.5 kg/m^2 in the gastric banding group, P = 0.01]) compared laparoscopic gastric bypass versus laparoscopic adjustable gastric banding. It found that gastric bypass significantly increased excess-weight loss at 4 years (% excess-weight lost: 68% with gastric bypass *v* 45% with gastric banding; P <0.05). [39]

Gastric bypass versus biliopancreatic diversion:
We found one systematic review (search date 2008), which identified no RCTs comparing gastric bypass versus biliopancreatic diversion [37] and one subsequent RCT. [40] The subsequent RCT (60 people with a BMI of 50–60 kg/m^2) compared laparoscopic gastric bypass versus laparoscopic biliopancreatic diversion with duodenal switch. [40] It found significantly greater excess BMI loss with biliopancreatic diversion with duodenal switch compared with gastric bypass at 1 year (excess BMI loss: 75% with biliopancreatic diversion with duodenal switch *v* 54% with gastric bypass; P <0.001). [40]

Gastric bypass versus sleeve gastrectomy:
We found one systematic review (search date 2008), [37] which identified one small RCT. The RCT (32 people with BMI >35 kg/m^2 [mean BMI >45.0 kg/m^2 in both groups]) found that sleeve gastrectomy significantly increased excess-weight loss at 1 year compared with gastric bypass (% excess-weight lost: 60.5% with gastric bypass *v* 69.7% with sleeve gastrectomy; P = 0.05). [37]

Proximal versus distal gastric bypass:
We found three RCTs comparing proximal versus distal laparoscopic gastric bypass. [41] [42] [43]

The first RCT (48 people with mean BMI 44.9 kg/m^2) found no significant difference in mean weight or mean excess-weight loss between proximal and distal gastric bypass at up to 2 years' follow-up (mean weight at 1 year: 76.3 kg with proximal *v* 79.0 kg with distal; mean weight at 2 years: 90 kg with proximal *v* 83.2 kg with distal; mean excess-weight lost: results displayed graphically; differences reported as not significant; P values not reported). [41]

The second RCT (133 people with BMI >40 kg/m^2) found no significant difference in mean weight loss, change in BMI, or percentage of excess-weight loss over time between proximal and distal gastric bypass at up to 3 years of follow-up (reported as not significant; absolute results presented graphically). [42] A larger proportion of people with a BMI >50 kg/m^2 in the distal gastric bypass group had greater success — defined by number achieving loss of >50% excess weight — at 18 months but not at 24 or 36 months compared with the proximal gastric bypass group (results displayed graphically; differences reported as not significant; P value not reported).

The third RCT (105 people with BMI 50 kg/m^2 or more) found no significant difference between proximal and distal gastric bypass in excess-weight loss at 4 years (mean % excess-weight lost: 70% with proximal *v* 74% with distal; reported as not significant; P value not reported). [43]

Open versus laparoscopic gastric bypass:
We found one systematic review (search date 2008; 4 RCTs, 360 people) comparing open versus laparoscopic gastric bypass. [37] The review did not pool data and so we report data from the individual RCTs identified: data reported are as reported in the review. [37] One RCT was reported as only an abstract and is not discussed further.

The first RCT (155 people with BMI 40–60 kg/m^2) identified by the review found no significant difference between open and laparoscopic techniques in excess-weight loss at 3 years (% excess-weight lost: 77% with laparoscopic gastric bypass *v* 67% with open gastric bypass; reported as non-significant; P value not reported). [37]

The second RCT (50 people with BMI >40 kg/m^2) identified by the review found that weight loss at 1 year was similar in each group (weight loss: 41 kg with open *v* 39 kg with laparoscopic; significance not assessed). [37]

The third RCT (104 people with morbid obesity) identified by the review found no significant difference in weight loss at a mean follow-up of 23 months between open and laparoscopic techniques (weight loss displayed graphically; between-group difference reported as not significant; P value not reported). [37]

Harms:

One systematic review (search date 2003) found that gastric bypass resulted in a 30-day mortality of 1.0% in comparative studies (95% CI 0.5% to 1.9%; 15 RCTs and non-randomised controlled trials, 907 people) and 0.3% in case series (95% CI 0.2% to 0.4%; 50 case series, 11,290 people). [38] Adverse effects were common, and included surgical complications (19%), nutritional and electrolyte abnormalities (17%), and GI symptoms (17%). [38]

Gastric bypass versus vertical banded gastroplasty:
The review did not pool data on adverse effects of surgeries. [37] Four RCTs identified by the review comparing gastric bypass versus vertical banded gastroplasty reported no deaths. [37] One RCT identified by the review reported no deaths with vertical banded gastroplasty, but two deaths (10%) with gastric bypass, which occurred after 3 days and 12 months, were caused by presumed arrhythmia.

One RCT identified by the review found that gastric bypass significantly increased the rate of early postoperative complications (including anastomotic leakage, abdominal abscess, and GI bleeding) compared with vertical banded gastroplasty (7/40 [18%] with gastric bypass *v* 1/40 [3%] with vertical banded gastroplasty; P <0.05). [44] Another RCT identified by the review found no significant difference between interventions in re-operation rates or perioperative complications (re-operation: 5/37 [14%] with gastric bypass *v* 1/46 [2%] with vertical banded gastroplasty; P = 0.08; minor bleeding: 2/37 [5%] with gastric bypass *v* 4/46 [9%] with vertical banded gastroplasty; suspected leakage: 1/37 [2.7%] with gastric bypass *v* 1/46 [2.2%] with vertical banded gastroplasty; difference reported as not significant for all outcomes; P values not reported for minor bleeding or suspected leakage). [45]

Gastric bypass versus gastric banding:
The RCT identified by the review reported no deaths. [37] The RCT found similar rates of re-operation for each technique (3/24 [13%] with gastric bypass *v* 4/26 [15%] with gastric banding; significance not assessed). People in the gastric banding group had re-operation for inadequate weight loss or pouch dilation. Reasons were not specified for re-operations in the gastric bypass group. Early and late complication rates were similar among procedures.The subsequent RCT reported that early complications were significantly more common in the gastric bypass group compared with the gastric banding group (22% with gastric bypass *v* 7% with gastric banding; P = 0.01). Early minor complications were significantly more common in the gastric bypass group (15% with gastric bypass *v* 5% with gastric banding; P = 0.02). Late complications were significantly more common in the gastric bypass group compared with the gastric banding group (39% with gastric bypass *v* 12% with gastric banding; P <0.01). [39]

Gastric bypass versus biliopancreatic diversion:
The RCT comparing laparoscopic gastric bypass versus laparoscopic biliopancreatic diversion with duodenal switch reported that mean operating time was significantly less with gastric bypass (91 minutes for gastric bypass *v* 206 minutes for biliopancreatic diversion with duodenal switch; P <0.001). [40] The RCT found no significant difference between groups in early or late complications (early complications: 7 with biliopancreatic diversion with duodenal switch *v* 4 with gastric bypass; P = 0.32; late complications: 9 with biliopancreatic diversion with duodenal switch *v* 4 with gastric bypass; P = 0.12). [40] In a subsequent article from this RCT reporting vitamin status, biliopancreatic diversion with duodenal switch resulted in significantly more vitamin A and D deficiencies in the first year after surgery and thiamine deficiency in the first months after surgery compared with gastric bypass. [46]

Gastric bypass versus sleeve gastrectomy:
The RCT identified by the review reported no deaths and no intraoperative or postoperative complications. [37] No other details were reported.

Proximal versus distal gastric bypass:
The first RCT reported no deaths in either group. [41] It found no significant difference in overall complication rates between proximal and distal gastric bypass (figures not reported; reported as not significant; P value not reported). However, the incidence of internal hernias was significantly lower with proximal bypass compared with distal bypass (0/25 [0%] with proximal bypass *v* 4/23 [17%] with distal bypass; P = 0.029). [41] The second RCT reported one death in the proximal gastric bypass group and one death in the distal gastric bypass group within the first 30 days. [42] It gave no other information on complications. The third RCT reported no deaths in either group. [43] The RCT reported that rates of re-operation were similar in each group (2/57 [4%] with proximal bypass *v* 1/48 [2%] with distal bypass; significance not assessed).

Open versus laparoscopic gastric bypass:
The RCTs identified by the review reported 4 postoperative deaths: one caused by malignant hyperthermia; one caused by possible pulmonary thromboembolism (laparoscopic); one caused by intestinal obstruction (laparoscopic); and one caused by evisceration. [37] The first RCT found no significant difference between open and laparoscopic bypass in the proportion of people who had major surgical complications (9% with open gastric bypass *v* 8% with laparoscopic gastric bypass; absolute numbers not reported; P = 0.78). However, this RCT found that open gastric bypass was associated with a significantly higher rate of incisional hernia (22/57 [39%] with open gastric bypass *v* 3/59 [5%] with laparoscopic gastric bypass; P <0.01). In all three RCTs identified by the review, minor complications (including vomiting, colicky pain, and wound infection) were not significantly different between groups. [37]

The second RCT found that open gastric bypass was associated with a significantly higher rate of late complications (including eventrations, abscess, intestinal obstruction, and pancreatitis) compared with laparoscopic gastric bypass (12/51 [24%] with open gastric bypass *v* 6/53 [11%] with laparoscopic gastric bypass; P <0.05). [37] Operating time was significantly longer for the laparoscopic procedure in two of the RCTs (first RCT: 195 minutes with open *v* 225 minutes with laparoscopic; P <0.001; second RCT: 85 minutes with open *v* 150 minutes with laparoscopic), but it was significantly longer for the open procedure in one RCT (201 minutes with open *v* 186 minutes with laparoscopic: P <0.05). [37] Hospital stay was significantly shorter for the laparoscopic procedure (4–8 days with open *v* 3–5 days with laparoscopic; P <0.05 in 2 RCTs). [37]

Reinforcement of staple lines in gastric bypass versus non-reinforcement:
We found three RCTs that evaluated reinforcement of staple lines in gastric bypass surgery. The first RCT (34 people with BMI of 40–60 kg/m^2) evaluated glycolide copolymer staple-line reinforcement sleeves versus non-reinforcement during laparoscopic gastric bypass. [47] The RCT found that reinforcement of the staple lines was associated with significantly fewer bleeding sites during

construction of the gastric pouch, the division of the jejunum, and the division of the jejunal mesenteric tissue (gastric pouch: 2.5 without reinforcement *v* 0.4 with reinforcement; division of the jejunum: 0.6 without reinforcement *v* 0.2 with reinforcement; division of the jejunal mesenteric tissue: 0.8 without reinforcement *v* 0 with reinforcement; P <0.01 for all comparisons). One person in the non-reinforcement arm had postoperative GI haemorrhage requiring transfusion and re-operation. [47]

The second RCT (48 people with BMI >35 kg/m^2) evaluated polyglycolide acid and trimethylene carbonate staple-line reinforcement versus non-reinforcement during laparoscopic gastric bypass. [48] The RCT found that, compared with non-reinforcement, reinforcement of staple lines was associated with a significantly shorter operation time (average time: 115 minutes with reinforcement *v* 150 minutes without reinforcement; P = 0.03), and significantly higher postoperative haemoglobin levels (mean haemoglobin level: 12.5 g/dL with reinforcement *v* 11.1 g/dL without reinforcement; P = 0.0156). No patients required re-operation or transfusion in either group.

The third RCT (340 people with BMI 40–50 kg/m^2) evaluated the use of biological fibrin sealant versus no sealant in laparoscopic gastric bypass. [49] The RCT found that the use of fibrin sealant resulted in fewer gastrojejunal anastomotic leaks; however, the difference was not significant (1 with fibrin sealant *v* 3 without fibrin sealant, P reported as not significant). The overall re-operation rate for early complications (<30 days) was significantly lower in the fibrin sealant group (1 with fibrin sealant *v* 7 without fibrin sealant, P = 0.001). The complications leading to re-operation included gastrojejunal anastomotic leak, internal hernia, and gastrojejunal anastomotic bleeding. There were no differences between the two groups in operative time, postoperative hospital stay, or time to oral diet. [49]

Comment: None.

OPTION GASTRIC BANDING

Weight loss

Compared with gastric bypass Gastric banding seems less effective at increasing weight loss at 5 years (high-quality evidence).

Compared with vertical banded gastroplasty Gastric banding may be less effective at increasing weight loss at 3 to 7 years (very low-quality evidence).

Compared with sleeve gastrectomy Gastric banding may be less effective at increasing weight loss at 1 and 3 years (low-quality evidence).

Open versus laparoscopic gastric banding We don't know whether open or laparoscopic gastric banding is more effective at increasing weight loss at 12 months (low-quality evidence).

Note

We found no clinically important results from RCTs about gastric banding compared with biliopancreatic diversion in people with obesity.

For GRADE evaluation of interventions for obesity in adults, **see table, p 24 .**

Benefits: One systematic review (search date 2003) found that gastric banding resulted in a mean weight loss of 30.2 kg (95% CI 28.0 kg to 32.4 kg; 27 RCTs, non-randomised controlled trials and case series; 5562 people) at 12-month follow-up and 34.8 kg (95% CI 29.5 kg to 40.1 kg; 17 RCTs, non-randomised controlled trials and case series; 3076 people) at 36-month follow-up and beyond. [38]

Gastric banding versus gastric bypass:

See benefits of gastric bypass, p 13 .

Gastric banding versus vertical banded gastroplasty:

We found one systematic review (search date 2008; 3 RCTs, 259 people) [37] and one subsequent paper reporting long-term follow-up for one of the RCTs included in the review. [50] The review did not pool data and so we report data separately from the individual RCTs. Data reported are as reported in the review. [37]

The first RCT (59 adults with BMI 40 kg/m^2 or more or BMI 37 kg/m^2 or more with associated comorbidity) identified by the review found that the gastric banding group had lost less weight at 1 year compared with the vertical banded gastroplasty group (change in mean weight from baseline: from 124 kg to 98 kg with gastric banding *v* from 123 kg to 82 kg with vertical banded gastroplasty; significance not assessed). However, at 5 years, the gastric banding group had lost more weight

(from 124 kg to 81 kg with gastric banding *v* from 123 kg to 88 kg with vertical banded gastroplasty; significance not assessed). [37]

The second RCT (100 adults with BMI 40–50 kg/m^2) found that a significantly smaller proportion of people achieved an excellent or good result (defined as residual excess weight of <50%) at 2 years in the laparoscopic gastric banding group compared with the laparoscopic vertical banded gastroplasty group (35% with gastric banding *v* 74% with vertical banded gastroplasty; absolute numbers not reported; P <0.001). There was no significant difference between groups in excellent or good result rates at 3 years, although the proportion of people classed as having an excellent or good result was smaller with gastric banding (25% with gastric banding *v* 63% with vertical banded gastroplasty; P = 0.056). The RCT also found no significant difference between the two surgeries in excess-weight loss at 2 and 3 years (% excess-weight lost: at 2 years: 41% with gastric banding *v* 64% with vertical banded gastroplasty; at 3 years: 39% with gastric banding *v* 59% with vertical banded gastroplasty; reported as not significant; P values not reported). [37]

The long-term follow-up of this RCT [50] found that at 3, 5, and 7 years percentage excess-weight loss was significantly lower with gastric banding compared with vertical banded gastroplasty (3 years: 41.8% with gastric banding *v* 60.9% with vertical banded gastroplasty; 5 years: 33.2% with gastric banding *v* 57.0% with vertical banded gastroplasty; 7 years: 29.9% with gastric banding *v* 53.1% with vertical banded gastroplasty; P <0.05 for all comparisons). [50]

The third RCT (100 adults with BMI >40 kg/m^2 or >35 kg/m^2 with associated comorbidity) found that laparoscopic gastric banding was significantly less effective at reducing excess weight at 1 and 2 years compared with open vertical banded gastroplasty (% excess-weight lost at 1 year: 53.3% with gastric banding *v* 71.1% with vertical banded gastroplasty; 2 years: 54.9% with gastric banding *v* 70.1% with vertical banded gastroplasty; P = 0.001 or less at both time points). [37]

Gastric banding versus sleeve gastrectomy:
We found one systematic review (search date 2008), which identified one RCT (80 adults with BMI >30 kg/m^2 [median BMI of 37 kg/m^2 in the gastric banding group and 39 kg/m^2 in the sleeve gastrectomy group]) comparing laparoscopic gastric banding versus laparoscopic isolated sleeve gastrectomy. [37]

The RCT found that weight loss and excess-weight loss at 1 and 3 years were significantly less with gastric banding compared with sleeve gastrectomy (median weight loss at 1 year: –14 kg with gastric banding *v* –26 kg with sleeve gastrectomy; P <0.0001; median weight loss at 3 years: –17 kg with gastric banding *v* –29.5 kg with sleeve gastrectomy; P <0.0001; % excess-weight lost at 1 year: 41.4% with gastric banding *v* 57.7% with sleeve gastrectomy; P = 0.0004; % excess-weight lost at 3 years: 48% with gastric banding *v* 66% with sleeve gastrectomy; P = 0.0025). [37]

Open versus laparoscopic gastric banding:
We found one systematic review (search date 2008), which identified one RCT (50 adults with BMI >40 kg/m^2) comparing open versus laparoscopic gastric banding. [37] The RCT found no significant difference in weight loss at 12 months between open and laparoscopic gastric banding (weight loss: –34.4 kg with open *v* –35.0 kg with laparoscopic gastric banding; reported as not significant; P value not reported).

Harms:

One systematic review (search date 2003) found that gastric banding resulted in a 30-day mortality of 0.4% in comparative studies (95% CI 0.01% to 2.1%; 6 RCTs and non-randomised controlled trials; 268 people) and 0.02% in case series (95% CI 0% to 0.78%; 35 case series, 9222 people). [38] Adverse effects were common and included surgical complications (13.2%), re-operations (7.7%), and GI symptoms (7.0%).

Gastric banding versus gastric bypass:
See harms of gastric bypass, p 13 .

Gastric banding versus vertical banded gastroplasty:
The review did not pool data on adverse effects. [37]

The first RCT identified by the review reported one death from each group during the follow-up period, but neither death was attributed to the surgery. Re-operations occurred in 10/27 (37%) people having vertical banded gastroplasty and 3/26 (12%) people having gastric banding. Gastro-oesophageal reflux was more common in people having vertical banded gastroplasty compared with people having gastric banding (4/27 [15%] with gastroplasty *v* 3/26 [12%] with gastric banding; significance not assessed). [37]

The second RCT identified by the review reported no deaths in either arm. [37] The RCT found that gastric banding significantly increased the proportion of people who required re-operation compared with vertical banded gastroplasty (12/49 [25%] with gastric banding *v* 0/50 [0%] with vertical banded gastroplasty; P <0.05). It also found that gastric banding significantly increased late complications, such as pouch dilatation, pouch to fundus fistula, symptomatic reflux disease, and gastric bezoar compared with vertical banded gastroplasty (16/49 [33%] with gastric banding *v* 7/50 [14%] with vertical banded gastroplasty; P <0.001). [37]

The long-term follow-up of this RCT reported one death in the vertical banded gastroplasty group due to street accident. [50] Long-term complications were significantly higher in the gastric banding group at 3 years but not at 5 or 7 years (3 years: 37% with gastric banding *v* 16% with vertical banded gastroplasty; P <0.05; 5 years: 47% with gastric banding *v* 43% with vertical banded gastroplasty; P value reported as not significant; 7 years: 55% with gastric banding *v* 47% with vertical banded gastroplasty; P value reported as not significant). The re-operation rate was significantly higher for the gastric banding group at 3, 5, and 7 years (3 years; 29% with gastric banding *v* 2% with vertical banded gastroplasty; 5 years: 39% with gastric banding *v* 2% with vertical banded gastroplasty; 7 years: 47% with gastric banding *v* 8% with vertical banded gastroplasty; P <0.001 for all comparisons). [50]

The third RCT identified by the review reported two (2/50 [4%]) deaths in the vertical banded gastroplasty group, but none in the gastric banding group. [37] It found that perioperative complications were more common in the vertical banded gastroplasty group than in the gastric banding group (3/50 [6%] with gastric banding *v* 9/50 [18%] with vertical banded gastroplasty; significance not assessed) and that rate of late complications requiring further surgery was similar in each group (20/50 [40%] with gastric banding *v* 26/50 [52%] with vertical banded gastroplasty; significance not assessed). [37]

Gastric banding versus sleeve gastrectomy:
The RCT identified by the review reported no deaths in either arm. [37] Two people who had sleeve gastrectomy required re-operation for early postoperative complications (intraperitoneal bleed and gastric ischaemia), but no one in the gastric band group required re-operation for early postoperative complications (significance not assessed for between-group comparison). Late complications requiring surgery were more common in the gastric band group compared with the sleeve gastrectomy group (7/40 [18%] with gastric banding *v* 0/40 [0%] with sleeve gastrectomy; significance not assessed). [37]

Open versus laparoscopic gastric banding:
The RCT identified by the review reported no deaths in either arm. [37] It also found no significant difference in surgical complications between the two procedures (no further details given; reported as not significant; P value not reported). It found no significant difference between open gastric banding and laparoscopic gastric banding in rate of incisional hernia complications, but the rate was higher with open gastric banding (3/25 [12%] with open *v* 0/25 [0%] with laparoscopic gastric banding; reported as not significant; P value not reported). It also found that open laparoscopic gastric banding was associated with a significantly higher rate of readmission at 1 year and significantly increased duration of hospital stay in the first year compared with laparoscopic gastric banding (readmissions: 15/25 [60%] with open *v* 6/25 [24%] with laparoscopic gastric banding; P <0.05; mean days in hospital: 11.8 days with open *v* 7.8 days with laparoscopic gastric banding; P <0.05). [37]

Comment: None.

OPTION VERTICAL BANDED GASTROPLASTY

Weight loss
Compared with gastric banding Vertical banded gastroplasty may be more effective at increasing weight loss at 3 to 7 years (very low-quality evidence).

Compared with gastric bypass Vertical banded gastroplasty seems less effective at increasing weight loss at 1 to 3 years (moderate-quality evidence).

Open compared with laparoscopic vertical banded gastroplasty We don't know whether open vertical banded gastroplasty is more effective at increasing weight loss at 12 months (low-quality evidence).

Note
There is a small risk of perioperative death with vertical banded gastroplasty, but GI symptoms and postoperative complications possibly requiring re-operation are common. Open vertical banded gastroplasty has a shorter operating time compared with laparoscopic banded gastroplasty. We found no clinically important results from RCTs about

vertical banded gastroplasty compared with non-surgical treatment, or compared with biliopancreatic diversion or sleeve gastrectomy in obese people.

For GRADE evaluation of interventions for obesity in adults, **see table, p 24 .**

Benefits: We found one systematic review (search date 2003), which found that vertical banded gastroplasty resulted in a mean weight loss of 32.2 kg (95% CI 29.9 kg to 34.4 kg; 21 RCTs, non-randomised controlled trials and case series; 2080 people; initial mean BMI not reported) at 12-month follow-up, and 32.0 kg (95% CI 27.7 kg to 36.4 kg; 18 RCTs, non-randomised controlled trials and case series; 1877 people; initial mean BMI not reported) at 36-month follow-up and beyond. [38]

Vertical banded gastroplasty versus gastric banding:
See benefits of gastric banding, p 17 .

Vertical banded gastroplasty versus gastric bypass:
See benefits of gastric bypass, p 13 .

Open versus laparoscopic vertical banded gastroplasty:
We found one systematic review (search date 2008), [37] which identified one small RCT (30 adults with BMI 40–50 kg/m^2). [51] The RCT found similar weight loss between open and laparoscopic vertical banded gastroplasty at 12 months (mean weight loss: 55% with open *v* 47% with laparoscopic; significance not assessed). [51]

Harms: One systematic review found that gastroplasty resulted in a 30-day mortality of 0.2% in controlled studies (95% CI 0% to 1.4%; 11 RCTs and non-randomised controlled trials; 401 people) and 0.3% in case series (95% CI 0.1% to 0.5%; 33 case series; 4091 people). [38] Adverse effects were common, and included surgical complications (24%), re-operations (11%), and GI symptoms (18%). [38]

Vertical banded gastroplasty versus gastric banding:
See harms of gastric banding, p 17 .

Vertical banded gastroplasty versus gastric bypass:
See harms of gastric bypass, p 13 .

Open versus laparoscopic vertical banded gastroplasty:
The RCT reported no deaths in either arm. [51] Operating time was significantly longer with laparoscopic compared with open vertical banded gastroplasty (2.10 hours with laparoscopic *v* 1.45 hours with open; P <0.002). [51] There was no significant difference between open and laparoscopic vertical banded gastroplasty in average hospital stay (4 days for both techniques; difference reported as not significant; P value not reported). Two people, one in each group, developed a fistula at the gastric partition that required re-operation. Two people having open gastroplasty developed abdominal-wall hernias at 12 months.

Comment: None.

OPTION BILIOPANCREATIC DIVERSION

Weight loss
Compared with gastric bypass Biliopancreatic diversion may be more effective at increasing excess-weight loss at 1 year (moderate-quality evidence).

Note
We found no clinically important results from RCTs about biliopancreatic diversion compared with non-surgical treatment, or compared with gastric banding, vertical banded gastroplasty, or sleeve gastrectomy in obese people.

For GRADE evaluation of interventions for obesity in adults, **see table, p 24 .**

Benefits: We found two systematic reviews (search dates 2003 [38] and 2008 [37]), which found no RCTs comparing biliopancreatic diversion versus other bariatric surgery techniques. One of the reviews identified three case series of biliopancreatic diversion (735 people) that assessed weight loss. [38] The review found that biliopancreatic diversion resulted in a mean weight loss of 51.9 kg (95% CI 45.1 kg to 58.8 kg; initial mean BMI not reported) at 12-month follow-up, and 53.1 kg (95% CI 47.4 kg to 58.8 kg; initial mean BMI not reported) at 36-month follow-up and beyond.

Biliopancreatic diversion versus gastric bypass:
See benefits of gastric bypass, p 13 .

Harms: We found no RCTs. The systematic review (search date 2003) of case series found that biliopancreatic diversion resulted in a 30-day mortality of 0.9% (95% CI 0.5% to 1.3%; 7 case series; 2808 people). [38] Adverse effects were common, and included surgical complications (6%), re-operations (4%), and GI symptoms (38%). [38]

Biliopancreatic diversion versus gastric bypass:
See harms of gastric bypass, p 13 .

Comment: None.

OPTION SLEEVE GASTRECTOMY

Weight loss
Compared with gastric banding Sleeve gastrectomy may be more effective at increasing weight loss at 1 and 3 years (low-quality evidence).

Compared with gastric bypass Sleeve gastrectomy seems more effective at increasing mean excess-weight loss at 1 to 2 years (moderate-quality evidence).

Note
We found no clinically important results from RCTs about sleeve gastrectomy compared with non-surgical treatment, or compared with vertical banded gastroplasty or biliopancreatic diversion in obese people.

For GRADE evaluation of interventions for obesity in adults, see table, p 24 .

Benefits:

Sleeve gastrectomy versus gastric banding:
See benefits of gastric banding, p 17 .

Sleeve gastrectomy versus gastric bypass:
See benefits of gastric bypass, p 13 .

Sleeve gastrectomy versus other bariatric surgery techniques:
We found two systematic reviews (search dates 2003 [38] and 2008 [37]), which identified no RCTs comparing sleeve gastrectomy versus other bariatric surgery techniques.

Harms:

Sleeve gastrectomy versus gastric banding:
See harms of gastric banding, p 17 .

Sleeve gastrectomy versus gastric bypass:
See harms of gastric bypass, p 13 .

Sleeve gastrectomy versus other bariatric surgery techniques:
We found no RCTs.

Comment: None.

GLOSSARY

Biliopancreatic diversion There are two different types of biliopancreatic diversion. Standard biliopancreatic diversion surgically removes the lower third of the stomach and then forms a connection with the remaining stomach pouch with a portion of the small intestine beyond where the stomach was originally attached. Biliopancreatic diversion with duodenal switch divides the stomach vertically and removes the left half, leaving the connection between the stomach and the duodenum of the small intestine intact. A length of intestine is also removed and the duodenum is reconnected further down the small intestine. The aim is to increase weight loss by reducing calories and decreasing nutrient absorption.

Bariatrics The branch of medicine concerned with the management (prevention and control) of obesity and its related diseases.

Body mass index (BMI) Expressed as weight in kilograms divided by height in metres squared (kg/m^2). In the US and UK, individuals with BMIs of 25 kg/m^2 to 30 kg/m^2 are considered overweight; those with BMIs above 30 kg/m^2 are considered obese.

Gastric bypass The roux-en-Y gastric bypass procedure involves dividing the stomach and creating a small pouch, which is then closed using several rows of staples. The remaining portion of the stomach is not removed but is "by-passed" and plays a diminished role in the digestive process. A Y-shaped portion of the small intestine is then attached to the pouch. The volume the new stomach pouch is capable of holding is about 25 g. The aim is to increase weight loss by reducing calories, altering GI appetite hormones, and decreasing nutrient absorption.

Gastroplasty Vertical banded gastroplasty involves stapling the front of the stomach to the back of the stomach along a vertical plane, partitioning the stomach into two unequal parts that connect through a small (about 0.5 cm) opening. This allows the partially digested food to move from the small stomach pouch into the rest of the stomach and then the intestines. The newly created upper pouch will only allow the person to consume small amounts of food at a time.

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Biliopancreatic diversion New evidence added. [40] Categorisation unchanged (Likely to be beneficial).

Diethylpropion New evidence added. [36] Categorisation unchanged (Unknown effectiveness) as there remains insufficient evidence to judge this intervention.

Gastric banding New evidence added. [50] Categorisation unchanged (Likely to be beneficial).

Gastric bypass New evidence added. [39] [40] [46] [49] Categorisation unchanged (Likely to be beneficial).

Sibutramine In October 2010, the FDA requested the withdrawal of sibutramine from the US market because of the increased risk of adverse cardiovascular events. Categorisation unchanged (Trade-off between benefits and harms).

Sibutramine plus orlistat In October 2010, the FDA requested the withdrawal of sibutramine from the US market because of the increased risk of adverse cardiovascular events. Categorisation changed from Unknown effectiveness to Trade off between benefits and harms.

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Disclaimer

TABLE **GRADE evaluation of interventions for Obesity in adults**

Important outcomes			Weight loss, mortality, adverse effects						
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
What are the effects of drug treatments in adults with obesity?									
At least 28 (at least 11,087) [14] [15] [16] [17] [18] [19] [20] [21]	Weight loss	Orlistat *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results in 1 systematic review (number of people in analysis not reported)
At least 26 (at least 10,095) [14] [15] [16] [17] [18] [19] [20] [21]	Adverse effects	Orlistat *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
6 (368) [22]	Weight loss	Phentermine *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
At least 16 (at least 5508) [16] [26] [27] [28] [29] [30]	Weight loss	Sibutramine *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for methodological issues (for inclusion of unpublished studies in 1 systematic review and combined analysis of weight loss and maintenance in 1 systematic review)
5 (795) [31]	Weight loss	Sibutramine *v* orlistat	4	–1	–1	0	0	Low	Quality point deducted for methodological issues (heterogeneity among RCTs and short follow-up in some included RCTs [<4 months]). Consistency point deducted for conflicting results for different populations
1 (89) [35]	Weight loss	Sibutramine plus orlistat *v* orlistat	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
2 (123) [23] [35]	Weight loss	Sibutramine plus orlistat *v* sibutramine	4	–3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and poor follow-up
1 (69) [36]	Weight loss	Diethylpropion v placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (69) [36]	Adverse effects	Diethylpropion v placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
What are the effects of bariatric surgery in adults with morbid obesity?									
5 (3757) [37]	Weight loss	Bariatric surgery *v* non-surgical treatments	4	–1	0	–1	0	Low	Quality point deducted for inclusion of observational data. Directness point deducted for restricted population (predominantly white women) that may affect generalisability of results
5 (351) [37]	Weight loss	Gastric bypass *v* vertical banded gastroplasty	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
2 (238) [37] [39]	Weight loss	Gastric bypass *v* gastric banding	4	0	0	0	0	High	
1 (60) [40]	Weight loss	Gastric bypass v biliopancreatic diversion	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (32) [37]	Weight loss	Gastric bypass *v* sleeve gastrectomy	4	–1	0	0	0	Moderate	Quality point deducted for sparse data

Important outcomes			Weight loss, mortality, adverse effects						
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
3 (296) [41] [42] [43]	Weight loss	Proximal *v* distal gastric bypass	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
3 (309) [37]	Weight loss	Open *v* laparoscopic gastric bypass	4	–2	0	0	0	Low	Quality points deducted for incomplete reporting of results and for not carrying out a between-group statistical assessment
3 (259) [37] [50]	Weight loss	Gastric banding *v* vertical banded gastroplasty	4	–2	–1	0	0	Very low	Quality points deducted for incomplete reporting and not carrying out a between-group statistical assessment. Consistency point deducted for different results for different outcomes and at different time frames
1 (80) [37]	Weight loss	Gastric banding *v* sleeve gastrectomy	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for inclusion of people who were not morbidly obese, which may affect generalisability of results
1 (50) [37]	Weight loss	Open *v* laparoscopic gastric banding	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (30) [51]	Weight loss	Open *v* laparoscopic vertical banded gastroplasty	4	–2	0	0	0	Low	Quality points deducted for sparse data and for not carrying out a statistical assessment

Type of evidence: 4 = RCT; 2 = Observational.
Consistency: similarity of results across studies.
Directness: generalisability of population or outcomes.
Effect size: based on relative risk or odds ratio.