

Obesity 1

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Key Messages

Drug treatments in adults with obesity

- **Diethylpropion** One systematic review found that, in people having lifestyle interventions, diethylpropion promoted modest weight loss compared with placebo in obese adults. The review provided insufficient evidence to compare diethylpropion versus other agents. We found two case reports describing pulmonary hypertension and psychosis with diethylpropion. We found insufficient evidence on weight regain and long term safety. A European Commission review concluded that a link between diethylpropion and heart and lung problems could not be excluded.
- **Fluoxetine** One systematic review found that, in people having lifestyle interventions, fluoxetine promoted modest weight loss compared with placebo in obese adults. We found insufficient evidence on weight regain and long term safety of fluoxetine in obesity. One systematic review of antidepressant treatment found an association between selective serotonin reuptake inhibitors such as fluoxetine and uncommon but serious adverse events, including bradycardia, bleeding, granulocytopenia, seizures, hyponatraemia, hepatotoxicity, serotonin syndrome, and extrapyramidal effects.
- **Mazindol** One systematic review found that, in people having lifestyle interventions, mazindol promoted modest weight loss compared with placebo in obese adults. The review provided insufficient evidence to compare mazindol versus other agents. We found one case report of pulmonary hypertension diagnosed 1 year after stopping treatment with mazindol. We found one case series of mazindol in people with stable cardiac disease that reported cardiac events such as atrial fibrillation and syncope. We found insufficient evidence on weight regain and long term safety.
- **Orlistat** Systematic reviews and subsequent RCTs found that, in people on a low calorie diet, orlistat modestly increased weight loss at 6–12 months compared with placebo in obese adults, in both those who did and who did not have diabetes, hyperlipidaemia, and hypertension. One RCT in obese people with hypercholesterolaemia found that orlistat plus fluvastatin increased weight loss compared with orlistat or fluvastatin alone. Another RCT found that orlistat was less effective than sibutramine in achieving weight loss. Adverse effects such as oily spotting from the rectum, flatulence, and faecal urgency occurred in a high proportion of people taking orlistat. We found insufficient evidence on weight regain and long term safety.
- **Phentermine** One systematic review found that, in people having lifestyle interventions, phentermine promoted modest weight loss compared with placebo in obese adults. RCTs identified by the review provided insufficient evidence to compare phentermine versus other agents. We found insufficient evidence on weight regain and long term safety with phentermine. A European Commission review concluded that a link between phentermine and heart and lung problems could not be excluded.
- **Sibutramine** Systematic reviews and subsequent RCTs found that, in people having dietary interventions with or without exercise, sibutramine promoted modest weight loss at 8 weeks, 6 months, and 1 year compared with placebo in obese adults, in both those who did and who did not have diabetes, hypertension, hyperlipidaemia, or binge eating disorder. RCTs in obese adults who had lost weight by taking sibutramine found limited evidence that sibutramine was more effective than placebo for weight maintenance. Other RCTs found that weight regain occurred when sibutramine was discontinued. One RCT found that sibutramine achieved greater weight loss than orlistat or

metformin. RCTs provided insufficient evidence to compare sibutramine versus other agents. Sibutramine was temporarily suspended from the market in Italy for use in obesity because of concerns about severe adverse reactions, including arrhythmias, hypertension, and two deaths resulting from cardiac arrest. Two RCTs found no significant difference in the incidence of valvular heart disease between sibutramine and placebo, although these trials may have lacked power to detect a clinically important difference.

- **Sibutramine plus orlistat (insufficient evidence to compare with sibutramine alone)** One RCT provided insufficient evidence to compare sibutramine plus orlistat versus sibutramine alone.

Bariatric surgery in adults with morbid obesity

- **Gastric bypass (increased weight loss compared with gastroplasty or gastric banding)** RCTs provided moderate evidence that gastric bypass promoted greater weight loss than either gastroplasty or gastric banding. Five RCTs identified by a systematic review found that gastric bypass increased weight loss compared with horizontal gastroplasty. Two RCTs identified by the review found that gastric bypass increased weight loss at 1–3 years compared with vertical banded gastroplasty but another two RCTs found no significant difference between the procedures. One small RCT identified by the review found limited evidence of greater weight loss with gastric bypass than with gastric banding or vertical banded gastroplasty. Another small RCT identified by the review found that gastric bypass increased the proportion of people with 50% weight loss at 18 months compared with vertical banded gastroplasty or gastrogastrostomy. Perioperative mortalities were similar for these procedures. Postoperative complications were common and varied by type of procedure performed.
- **Laparoscopic bariatric surgery (reduced wound infections and risk of incisional hernias compared with open bariatric surgery, no significant difference in weight loss)** Five RCTs found no significant difference in weight loss between open and laparoscopic bariatric procedures. The RCTs found consistent evidence that laparoscopic surgery reduced the incidence of wound and incisional hernia complications compared with open surgery. They found more limited evidence that laparoscopic procedures decreased length of hospital stay compared with open procedures; but data are insufficient to draw conclusions about other complication rates.
- **Bariatric surgery (more effective for clinically important weight loss in morbidly obese adults than non-surgical treatment but operative complication rates common)** One RCT and one cohort study in morbidly obese adults identified by three systematic reviews found that bariatric surgery (horizontal gastroplasty, vertical banded gastroplasty, gastric bypass, or gastric banding) was more effective than non-surgical treatment in increasing weight loss in people with morbid obesity. The cohort study found that, on average, bariatric surgery for obesity resulted in weight losses of 25–44 kg after 1–2 years (compared with matched participants who did not have surgery) and sustained weight loss of 20 kg up to 8 years later. The risk of death from bariatric surgery is estimated to be 0–1.5%. Operative and postoperative complications are common and vary with the type of bariatric procedure performed. The reviews identified no RCTs and we found no observational studies of sufficient quality comparing biliopancreatic diversion versus non-surgical treatment.

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- **Biliopancreatic diversion (no studies comparing biliopancreatic diversion versus other bariatric techniques)** Three systematic reviews identified no RCTs and we found no observational studies of sufficient quality comparing biliopancreatic diversion versus other bariatric procedures.
- **Gastric banding (less effective in reducing weight than gastric bypass; insufficient evidence to assess benefits and harms compared with gastroplasty)** One small RCT identified by a systematic review found limited evidence that gastric banding was less effective than gastric bypass in reducing weight. Two RCTs found inconclusive results regarding weight loss with gastric banding compared with vertical banded gastroplasty. There were no postoperative deaths in either RCT. Postoperative complications were common and varied by type of procedure performed. There is insufficient evidence to recommend one procedure over the other.
- **Gastroplasty (less effective in reducing weight than gastric bypass; insufficient evidence to assess benefits and harms compared with gastric banding)** Two RCTs found inconclusive results regarding weight loss with vertical banded gastroplasty compared with gastric banding. Five RCTs identified by a systematic review found that horizontal gastroplasty was less effective than gastric bypass for increasing weight loss. Four RCTs identified by the review found that vertical banded gastroplasty was less effective than gastric bypass in increasing weight loss at 1–3 years but another two RCTs found no significant difference between the procedures. Perioperative mortalities were similar for these procedures. Postoperative complications were common and varied by type of procedure performed. There is insufficient evidence to recommend one procedure over another.

DEFINITION Obesity is a chronic condition characterised by an excess of body fat. It is most often defined by the body mass index (see glossary, p 20) (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 BMIs between 25–30 kg/m^2 are categorised as overweight, and those with BMIs 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. A 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 in the USA 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 concomitant risk factors or 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 concomitant risk factors are candidates for bariatric surgery.

INCIDENCE/ PREVALENCE Obesity has increased steadily in many countries since 1900. In the UK in 2001, it was estimated that 21% of men and 24% of women were obese.⁴ In the past decade alone, the prevalence of obesity in the USA has increased from 22.9% between 1988 and 1994, to 30.5% between 1999 and 2000.⁵

AETIOLOGY/ RISK FACTORS Obesity is the result of long term mismatches in energy balance where daily energy intake exceeds daily energy expenditure.⁶ Energy balance is modulated by a myriad of factors, including metabolic rate, appetite, diet, and physical activity.⁷ 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 is more often attributed to environmental changes that promote excessive food intake and discourage physical activity.^{7,8} Less commonly, obesity may also be induced by drugs (e.g. high dose glucocorticoids), or be secondary to a variety of neuroendocrine disorders such as Cushing's syndrome and polycystic ovary syndrome.⁹

PROGNOSIS Obesity is a risk factor for several chronic diseases, including hypertension, dyslipidaemia, diabetes, cardiovascular disease, 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/m²) and among adults with the highest body weight (BMI > 35 kg/m²).² Results from five prospective cohort studies and 1991 national statistics suggest that the number of annual deaths attributable to obesity among US adults is about 280 000.¹⁰ Obese adults also 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}

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; adverse effects of treatment. We found no studies that assessed the primary outcome of reduction in mortality associated with obesity. 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.

METHODS *Clinical Evidence* search and appraisal April 2004. 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. We have excluded RCTs with greater than 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. Two systematic reviews^{13,14} and two cohort studies^{15,16} of bariatric surgery were published after the search date of our review. They are mentioned in the comments and will be reported in full in the next issue of *Clinical Evidence*.

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

OPTION SIBUTRAMINE

Systematic reviews and subsequent RCTs found that, in people having dietary interventions with or without exercise, sibutramine promoted modest weight loss at 8 weeks, 6 months, and 1 year compared with placebo in obese adults, in both those who did and who did not have diabetes, hypertension, hyperlipidaemia, or binge eating disorder. RCTs in obese adults who had lost weight by taking sibutramine found limited evidence that sibutramine was more effective than placebo for weight

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maintenance. Other RCTs found that weight regain occurred when sibutramine was discontinued. One RCT found that sibutramine achieved greater weight loss than orlistat or metformin. RCTs provided insufficient evidence to compare sibutramine versus other agents or sibutramine plus orlistat versus sibutramine alone. Sibutramine was temporarily suspended from the market in Italy for use in obesity because of concerns about severe adverse reactions, including arrhythmias, hypertension, and two deaths resulting from cardiac arrest. Two RCTs found no significant difference in the incidence of valvular heart disease between sibutramine and placebo, although these trials may have lacked power to detect a clinically important difference.

Benefits: **Sibutramine versus placebo:** We found one systematic review (search date 2002, 29 RCTs in people with body mass index (see glossary, p 20) 25–40 kg/m², some with diabetes, hypertension, hyperlipidaemia, or binge eating disorder)¹⁷ and one subsequent RCT.¹⁸ The review meta-analyzed data for groups of RCTs with similar study duration, method of analysis, and duration of follow up.¹⁷ All of the meta-analyses found that sibutramine significantly increased weight loss compared with placebo. The review found that sibutramine 10–15 mg daily significantly increased weight loss at 8–12 weeks compared with placebo (7 RCTs, 546 people; WMD –2.78 kg, 95% CI –3.29 kg to –2.26 kg). Trials of 16–24 weeks' duration, all comparing sibutramine 10–15 mg daily versus placebo, were meta-analyzed in three subgroups because of significant heterogeneity among the trials in methods of analysis. The weighted mean difference in weight loss between sibutramine and placebo ranged from –3.43 kg, 95% CI –4.50 to –2.36 to –6.03 kg, 95% CI –7.36 to –4.70 kg; people who completed the trial had the greatest weight loss. The review also found that sibutramine 10–15 mg daily significantly increased weight loss at 45–54 weeks compared with placebo (5 RCTs, 2188 people; WMD –4.45 kg, 95% CI –5.29 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 trials in obese adults who did not have co-morbidities.¹⁷ The subsequent RCT (60 obese adults with binge eating disorder) compared sibutramine 15 mg daily versus placebo for 12 weeks.¹⁸ It found that sibutramine significantly increased weight loss at 12 weeks compared with placebo (7.4 kg weight loss with sibutramine v 1.4 kg weight gain with placebo; P < 0.001). One RCT identified by the review assessed sibutramine for weight maintenance.¹⁷ Participants with greater than 5% weight loss at the completion of 6 months' treatment with sibutramine 10 mg daily were randomised to continue to receive sibutramine 10–20 mg daily or placebo for 18 months (467 people). The RCT was limited by only 56% follow up at 2 years. It found that sibutramine maintained significantly more weight loss at 2 years compared with placebo (WMD –4.0 kg, 95% CI –5.6 kg to –2.4). Two RCTs identified by the review assessed weight regain after discontinuation of treatment in people who had successful weight loss after 6 months' treatment with sibutramine. People regained 43% of lost body weight at 6 months (40 people) and 55% of lost body weight at 18 months (115 people).¹⁷

Sibutramine versus orlistat or metformin: We found no systematic review but found one RCT (150 obese women) comparing three

treatments: sibutramine 20 mg daily; orlistat (120 mg 3 times daily); and metformin (850 mg twice daily) for 6 months.¹⁹ All people were also instructed to follow a reduced calorie diet of 25 kcal/kg of ideal body weight. The RCT found that sibutramine achieved greater weight loss than either orlistat or metformin (−13.0 kg with sibutramine v −8.0 kg with orlistat v −9.0 kg with metformin; sibutramine v orlistat and sibutramine v metformin $P < 0.0001$). **Sibutramine versus other agents:** We found one systematic review (search date 1999), which identified no RCTs comparing sibutramine versus diethylpropion, fluoxetine, mazindol, orlistat, or phentermine.²⁰ **Sibutramine plus orlistat:** We found no systematic review but found one RCT (34 women who had completed 1 year of sibutramine plus lifestyle modification), which compared sibutramine 10–15 mg daily plus orlistat (120 mg 3 times daily) versus sibutramine plus placebo for weight maintenance.²¹ Only 76% of the women completed the study. Mean body weight did not change significantly in either group over a 16 week period (+0.1 kg with sibutramine plus orlistat v +0.5 kg with sibutramine plus placebo).

Harms:

Sibutramine versus placebo: We found one systematic review¹⁷ and two additional RCTs^{22,23} that assessed adverse effects of sibutramine. The review found that sibutramine increased blood pressure (mean increase: systolic blood pressure: −0.2 mm Hg at 8–12 weeks, range from −1.6 to +5.6 mm Hg at 16–24 weeks in several RCTs, and range from +4.6 mm Hg at 44–54 weeks; diastolic blood pressure: range from +1.6 mm Hg at 8–12 weeks, −0.8 to +1.7 mmHg at 16–24 weeks, and +2.8 mm Hg at 44–54 weeks in several RCTs).¹⁷ It also found that sibutramine significantly increased heart rate compared with placebo (increase in heart rate: 1.3 beats/minute at 8–12 weeks, 0.75–5.9 beats/minute at 16–24 weeks, and 5.9 beats/minute at 44–54 weeks).¹⁷ Sibutramine was also associated with increased levels in total and low density lipoprotein cholesterol levels at 16–24 weeks compared with placebo (increase in total cholesterol: −1.9 to +1.8 mg/dL; increase in low density lipoprotein cholesterol 0.6 to 2.6 mg/dL); but no increase at 44–54 weeks.¹⁷ Common adverse effects were headache, nausea, constipation, insomnia, and dry mouth, occurring in 20.4% of people taking sibutramine compared with 3.4% of people on placebo ($P < 0.01$).¹⁷ We found two RCTs that assessed the effects of sibutramine on heart valve function.^{22,23} 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.²² 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 did not report on efficacy. The second RCT (184 obese people) compared sibutramine 10 or 20 mg daily versus placebo.²³ It reported no change in valvular appearance on echocardiogram in any group (no statistical comparisons between or within groups reported).²³ We found no evidence about adverse effects after more than 1 year of treatment. Sibutramine was temporarily suspended from the market in Italy in March 2002 in response to 50 reported adverse reactions, including seven severe adverse reactions (tachycardia,

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hypertension, and arrhythmia) and two deaths resulting from cardiac arrest. The Central European Committee for Proprietary Medicinal Products (CPMP) completed a review of sibutramine in June 2002, and concluded that the risk benefit profile of sibutramine remains in favour of benefit; it therefore lifted the suspension in August 2002.²⁴ To date, searches of the websites of other regulatory authorities, including the Medicines Control Agency, UK; the Food and Drug Administration, USA; Health, Canada; and the Therapeutics Goods Administration, Australia, found that no other countries have taken any regulatory actions against the drug.

Sibutramine versus orlistat or metformin: The RCT reported dry mouth, insomnia, constipation, and hypertension with sibutramine, and abdominal discomfort with orlistat and metformin.¹⁹

Sibutramine versus other agents: The systematic review gave no information on adverse effects.²⁰ **Sibutramine plus orlistat:** The RCT found that people who received sibutramine plus orlistat experienced more soft stools, bowel movements, oily evacuation, and more faecal urge than sibutramine alone (soft stools: 50.0% with sibutramine plus orlistat v 9.1% with sibutramine alone; increased frequency of bowel movements: 50.0% with sibutramine plus orlistat v 9.1% with sibutramine alone; oily evacuation: 42.9% with sibutramine plus orlistat v 0% with sibutramine alone; more faecal urgency: 42.9% with sibutramine plus orlistat v 9.1% with sibutramine alone).²¹

Comment: Most of the people treated with sibutramine received additional dietary interventions, and many also have received an exercise intervention. The review suggested that weight loss with sibutramine is associated with both positive and negative changes in cardiovascular and metabolic risk factors.¹⁷ Sibutramine has been associated with increases in systolic and diastolic blood pressure, heart rate, and total as well as low density lipoprotein cholesterol; it has conversely been associated with modest decreases in triglyceride levels, fasting serum glucose levels, glycosylated haemoglobin levels, and modest increases in high density lipoprotein cholesterol levels.¹⁷

OPTION PHENTERMINE

One systematic review found that, in people having lifestyle interventions, phentermine promoted modest weight loss compared with placebo in obese adults. RCTs identified by the review provided insufficient evidence to compare phentermine versus other agents. We found insufficient evidence on weight regain and long term safety with phentermine. A European Commission review concluded that a link between phentermine and heart and lung problems could not be excluded.

Benefits: **Phentermine versus placebo:** We found one systematic review (search date 1999, 6 RCTs, 368 people) comparing phentermine 15–30 mg daily versus placebo in obese adults, with mean follow up of 13.2 weeks (range 2–24 weeks).²⁰ The review found that phentermine produced significantly more weight loss than placebo (effect size: < 0.6 [information presented graphically]; mean difference in weight loss between phentermine and placebo in the six

RCTs ranged from 0.6–6.0 kg). **Phentermine versus diethylpropion:** The review also found that phentermine significantly increased weight loss compared with diethylpropion (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).²⁰ **Phentermine versus mazindol:** See benefits of mazindol, p 9. **Phentermine versus other drugs:** The review found no RCTs comparing phentermine versus diethylpropion, fluoxetine, orlistat, or sibutramine.²⁰

Harms: The systematic review gave no information on adverse effects.²⁰ Phentermine given alone has not been associated with valvular heart disease.²⁵ 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.²⁶

Comment: Most of the people treated with phentermine received additional lifestyle interventions.²⁰ High withdrawal rates have been reported for phentermine.

OPTION MAZINDOL

One systematic review found that, in people having lifestyle interventions, mazindol promoted modest weight loss compared with placebo in obese adults. The review provided insufficient evidence to compare mazindol versus other agents. We found one case report of pulmonary hypertension diagnosed 1 year after stopping treatment with mazindol. We found one case series of mazindol in people with stable cardiac disease that reported cardiac events such as atrial fibrillation and syncope. We found insufficient evidence on weight regain and long term safety.

Benefits: **Mazindol versus placebo:** We found one systematic review (search date 1999, 22 RCTs, 906 people) comparing mazindol 1–3 mg daily versus placebo in obese adults with mean follow up of 11 weeks (range 2–20 weeks).²⁰ The review found that mazindol significantly increased weight loss compared with placebo (effect size: < 0.5; absolute data presented graphically; mean difference in weight loss between mazindol and placebo in the 22 RCTs ranged from 0.1–7.3 kg). **Mazindol versus other drugs:** The review also compared mazindol versus other agents.²⁰ Three RCTs identified by the review found no significant difference in weight loss between mazindol and diethylpropion (mean 6.7 kg with mazindol v 5.1 with diethylpropion; effect size: +0.31, 95% CI –0.07 to +0.69). One RCT identified by the review found that mazindol significantly increased weight loss compared with phentermine (mean 6.7 kg v 5.5 kg; effect size: 0.12, CI not reported). The review found no RCTs comparing mazindol versus diethylpropion, fluoxetine, orlistat, or sibutramine.

Harms: The systematic review gave no information on adverse effects.²⁰ We found a single case report of pulmonary hypertension diagnosed 12 months after stopping mazindol that had been taken for 10

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weeks.²⁷ One case series of mazindol in people with stable cardiac disease reported several cardiac events (3 episodes of atrial fibrillation and 2 of syncope in 15 people receiving mazindol for 12 weeks).²⁸ The frequency of serious adverse events with this agent remains unclear.

Comment: Most of the people treated with mazindol received additional lifestyle interventions.²⁰

OPTION DIETHYLPROPION

One systematic review found that, in people having lifestyle interventions, diethylpropion promoted modest weight loss compared with placebo in obese adults. The review provided insufficient evidence to compare diethylpropion versus other agents. We found two case reports describing pulmonary hypertension and psychosis with diethylpropion. We found insufficient evidence on weight regain and long term safety. A European Commission review concluded that a link between diethylpropion and heart and lung problems could not be excluded.

Benefits: **Diethylpropion versus placebo:** We found one systematic review (search date 1999, 9 RCTs, 353 people) comparing diethylpropion 75 mg daily versus placebo in obese adults with mean follow up of 17.6 weeks (range 6–52 weeks).²⁰ The review found that diethylpropion significantly increased weight loss compared with placebo (effect size: < 0.55 [information presented graphically]; mean difference in weight loss between diethylpropion and placebo in the 9 RCTs ranged from 1.6–11.5 kg). **Diethylpropion versus mazindol:** See benefits of mazindol, p 9. **Diethylpropion versus phentermine:** See benefits of phentermine, p 8. **Diethylpropion versus other drugs:** The review identified no RCTs comparing diethylpropion versus fluoxetine, orlistat, or sibutramine.²⁰

Harms: The systematic review gave no information on adverse effects.²⁰ Case reports have described pulmonary hypertension and psychosis in users of diethylpropion.^{29,30} The frequency of serious adverse events with diethylpropion remains unclear. A European Commission review of the risks and benefits of diethylpropion concluded that randomised trials do not adequately show efficacy for weight loss.²⁶ Although no new safety problems were identified with diethylpropion, the Commission commented that a link between diethylpropion and heart and lung problems could not be totally excluded.

Comment: Most of the people treated with diethylpropion received additional lifestyle interventions.²⁰

OPTION FLUOXETINE

One systematic review found that, in people having lifestyle interventions, fluoxetine promoted modest weight loss compared with placebo in obese adults. We found insufficient evidence on weight regain and long term safety of fluoxetine in obesity. One systematic review of antidepressant treatment found an association between selective

serotonin reuptake inhibitors such as fluoxetine and uncommon but serious adverse events, including bradycardia, bleeding, granulocytopenia, seizures, hyponatraemia, hepatotoxicity, serotonin syndrome, and extrapyramidal effects.

- Benefits:** **Fluoxetine versus placebo:** We found one systematic review (search date 1999, 11 RCTs, 1219 people) comparing fluoxetine 32.5–60.0 mg daily versus placebo in obese adults with mean follow up of 27.5 weeks (range 6–60 weeks).²⁰ The review found that fluoxetine produced significant weight loss compared with placebo (effect size: < 0.45 [information presented graphically]; mean difference in weight loss between fluoxetine and placebo in the 11 RCTs ranged from 0.2–7.4 kg). **Fluoxetine versus other drugs:** The review identified no RCTs comparing fluoxetine versus diethylpropion, mazindol, orlistat, phentermine, or sibutramine.²⁰
- Harms:** The systematic review gave no information on adverse effects.²⁰ One older systematic review (search date 1998) of antidepressant treatment (for other indications) found that selective serotonin reuptake inhibitors were associated with a 10–15% incidence of anxiety, diarrhoea, dry mouth, headache, and nausea.³¹ The review also found an association between selective serotonin reuptake inhibitors and uncommon but serious adverse events, including bradycardia, bleeding, granulocytopenia, seizures, hyponatraemia, hepatotoxicity, serotonin syndrome (see glossary, p 20), and extrapyramidal effects (see glossary, p 20).
- Comment:** Most of the people treated with fluoxetine received additional lifestyle interventions.²⁰

OPTION ORLISTAT

Systematic reviews and subsequent RCTs found that, in people on a low calorie diet, orlistat modestly increased weight loss at 6–12 months compared with placebo in obese adults, in both those who did and who did not have diabetes, hyperlipidaemia, and hypertension. One RCT in obese people with hypercholesterolaemia found that orlistat plus fluvastatin increased weight loss compared with orlistat or fluvastatin alone. Another RCT found that orlistat was less effective than sibutramine in achieving weight loss. A third RCT provided insufficient evidence to compare adding orlistat to sibutramine versus sibutramine alone. Adverse effects such as oily spotting from the rectum, flatulence, and faecal urgency occurred in a high proportion of people taking orlistat. We found insufficient evidence on weight regain and long term safety.

- Benefits:** **Orlistat versus placebo:** We found one systematic review (search date 2002),³² and one subsequent RCT³³ comparing orlistat versus placebo. The review (19 RCTs) meta-analyzed results from RCTs with similar study design, dose of orlistat, and duration of follow up.³² All of the meta-analyses found that orlistat at all doses significantly increased modest weight loss at 6 months to 1 year compared with placebo. For example, orlistat 60 or 120 mg 3 times daily significantly increased weight loss at 1 year compared with placebo (2 RCTs, 910 people: WMD –2.44 kg, 95% CI –3.40 kg to –1.47 kg with 60 mg; 3 RCTs, 1789 people: WMD –3.19 kg (95% CI –3.98 kg to –2.40 kg with 120 mg). However, the meta-analyses

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found no significant difference in weight loss at 3 months between orlistat and placebo. For example, one meta-analysis found no significant difference between orlistat 50–60 mg 3 times daily and placebo in weight loss at 3 months (2 RCTs, 133 people: WMD -1.24 kg, 95% CI -2.65 kg to $+0.16$ kg). Similar beneficial results were found comparing the efficacy of orlistat at greater and lesser durations of treatment. The review performed separate meta-analyses comparing orlistat versus placebo in people with defined obesity related comorbidities such as type 2 diabetes mellitus, hyperlipidaemia, or multiple cardiovascular risk factors (impaired glucose tolerance/diabetes, dyslipidaemia, or hypertension) and found similar results. The subsequent RCT (343 obese people with non-insulin dependent diabetes) found that orlistat (120 mg 3 times daily) significantly increased weight loss compared with placebo at 6 months (mean weight loss: 4.24 kg with orlistat v 2.58 with placebo; $P = 0.0003$).³³ The review identified one RCT comparing orlistat versus placebo for weight maintenance.³² After 6 months of diet alone, people received orlistat (30, 60, or 120 mg 3 times daily) or placebo for 1 year. The RCT found that orlistat 120 mg significantly reduced weight regain at 1 year compared with placebo. However, it found no significant difference in weight regain between orlistat at other doses and placebo (percentage of weight regained: 32.4% with orlistat 120 mg v 47.2% with orlistat 60 mg v 53.3% with orlistat 30 mg v 56.0% with placebo; $P < 0.001$ for orlistat 120 mg v placebo, P reported as non-significant for other doses, CI not reported).³² **Orlistat plus fluvastatin:** We found no systematic review but found one RCT (99 obese people with hypercholesterolaemia) that compared four treatments over 1 year: orlistat (120 mg 3 times daily); fluvastatin (80 mg 4 times daily); orlistat (120 mg 3 times daily) plus fluvastatin (80 mg 4 times daily); and placebo.³⁴ It found that orlistat plus fluvastatin significantly increased weight loss compared orlistat alone, fluvastatin alone, or placebo (mean weight loss: 11.4 kg with orlistat plus fluvastatin v 8.6 kg with orlistat v 8.0 kg with fluvastatin v 7.6 kg with placebo; $P < 0.05$). **Orlistat plus sibutramine:** See benefits of sibutramine, p 6. **Versus other drugs:** We found one systematic review (search date 1999), which identified no RCTs comparing orlistat versus diethylpropion, fluoxetine, mazindol, phentermine or sibutramine.²⁰ We found one subsequent RCT comparing orlistat versus sibutramine (see benefits of sibutramine, p 6).²¹

Harms:

Versus placebo: Gastrointestinal adverse events such as loose stools, increased defaecation, abdominal pain, nausea and vomiting, oily spotting from the rectum, flatulence, and faecal urgency were more common with orlistat than placebo (48–95% with orlistat 120 mg 3 times daily v 18–68% with placebo).³² The first subsequent RCT (343 people with type 2 diabetes mellitus) found that orlistat significantly increased gastrointestinal adverse effects and increased withdrawals because of adverse effects compared with placebo (gastrointestinal effects: 65% with orlistat v 37% with placebo; withdrawals: 4.7% with orlistat v 2.9% with placebo; P values not reported).³³ **Orlistat plus sibutramine:** See harms of sibutramine, p 7. **Versus sibutramine:** See harms of sibutramine, p 7.

Comment: People treated with orlistat also undertook a low calorie diet.³² Because of the high rates of gastrointestinal adverse effects associated with orlistat, authors have queried whether blinded evaluation is possible.²¹ At the end of a double blinded 16 week trial, 22/26 [85%] people correctly identified their treatment group.

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

OPTION BARIATRIC SURGERY VERSUS NON-SURGICAL TREATMENT

One RCT and one cohort study identified by three systematic reviews found that bariatric surgery (horizontal gastroplasty, vertical banded gastroplasty, gastric bypass, or gastric banding) was more effective than non-surgical treatment in increasing weight loss in people with morbid obesity. The cohort study found that, on average, bariatric surgery for obesity resulted in weight losses of 25–44 kg after 1–2 years (compared with matched participants who did not have surgery) and sustained weight loss of 20 kg up to 8 years later. The risk of death from bariatric surgery is estimated to be 0 to 1.5%. Operative and postoperative complications are common and vary with the type of bariatric procedure performed. The reviews identified no RCTs and we found no observational studies of sufficient quality comparing biliopancreatic diversion versus non-surgical treatment.

Benefits: We found three systematic reviews of bariatric surgery (search dates 2001,³⁵ 2003^{36,37}), all of which identified the same single RCT and multicentre cohort study with matched controls comparing bariatric surgery (horizontal gastroplasty (see glossary, p 20), vertical banded gastroplasty, gastric bypass (see glossary, p 20), or gastric banding (see glossary, p 20)) versus non-surgical treatment. The RCT and cohort study both suggested that bariatric surgery was more effective than non-surgical treatment for weight loss in adults with morbid obesity. The RCT (57 adults \geq 60% overweight) identified by the reviews compared horizontal gastroplasty versus a very low calorie diet (500 kcal, 34 g protein daily) for 24 months. It found that horizontal gastroplasty significantly reduced body weight at 24 months compared with a very low calorie diet (32 kg with gastroplasty v 9 kg with very low calorie diet; $P < 0.05$). However, it found no significant difference in the proportion of people who had a net weight loss of 10 kg at 5 years (30% with horizontal gastroplasty v 17% with a very low calorie diet; P value reported as non-significant, CI not reported). The multicentre cohort study (2188 people) identified by the reviews^{35–37} compared bariatric surgery versus usual care.³⁸ Eligible participants self selected either a bariatric surgery group or a non-surgical (usual care) group. Each person who selected surgical treatment was matched on 18 clinical variables with a person from the non-surgical 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 cohort study found that people who had surgery lost significantly more weight than people receiving usual care at 1 year

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(mean weight loss: 44.0 kg with gastric bypass [68 people] v 30.7 kg with vertical banded gastroplasty [834 people] v 25.8 kg with gastric banding [255 people] v 1.6 kg with usual care [1031 people]; $P < 0.0001$ for all surgical groups v usual care). The differences in weight loss between groups remained significant at 8 years (mean percentage of body weight lost: 16.3% with surgery [232 people] v 0.9% weight gained with usual care [251 people]; mean difference in weight 20.7 kg; $P < 0.01$).

Harms:

The RCT reported no deaths related to surgery and no-one required re-operation.³⁵⁻³⁷ As of 31 January 2001 the cohort study reported five postoperative deaths in 2010 people (0.25%); three deaths owing to leakage, one owing to technical mistake during laparoscopic surgery, and one owing to postoperative myocardial infarction.³⁸ It reported that 2.2% of people required re-operation. One systematic review evaluated 38 surgical case series of bariatric surgery, which included people with both substantial comorbid conditions and mild health problems, and found that perioperative mortalities were low and similar across bariatric procedures: 0-1.5% among people who received gastric bypass, gastroplasty, or gastric banding.³⁷ Perioperative complications were common, including: subphrenic abscess (7%), atelectasis or pneumonia (4%), wound infection (4%), and pulmonary symptoms (6.2%).

Comment:

The cohort study will not be able to report on total mortality until 2004-2006.³⁸ Horizontal gastroplasty is less often performed worldwide, because of evidence of greater weight loss and comparable complication rates with gastric bypass. Two systematic reviews were published after the search date of our review.^{13,14} These reviews did not identify any additional RCTs comparing bariatric surgery versus non-surgical techniques. Two cohort studies were published after our search date, which compared bariatric surgery versus non-surgical treatment in morbidly obese adults.^{15,16} The first study (1035 people having surgery and 5746 having non-surgical treatment) found significantly lower mortality over a mean of 5.3 years in people having surgery compared with people having non-surgical treatment (0.68% with surgery v 6.17% with non-surgical treatment; RR 0.11; 95% CI 0.04 to 0.27).¹⁵ The second cohort study (3328 people having surgery and 62 781 having non-surgical interventions) also found significantly lower mortality at 15 years' follow up in people having surgery compared with non-surgical treatment (12% with surgery v 16% with non-surgical treatment; adjusted HR 0.67; 95% CI 0.54 to 0.85).¹⁶ This study also found 2% mortality at 30 days in people having surgery.¹⁶

OPTION

GASTRIC BANDING VERSUS OTHER BARIATRIC SURGICAL TECHNIQUES

One small RCT identified by a systematic review found limited evidence that gastric banding was less effective than gastric bypass in reducing weight. Two RCTs found inconclusive results regarding weight loss with gastric banding compared with vertical banded gastroplasty. There were no postoperative deaths in either RCT. Postoperative complications were common and varied by type of procedure performed. There is insufficient evidence to recommend one procedure over the other.

Benefits: **Gastric banding versus gastric bypass:** See glossary, p 20. See benefits of gastric bypass, p 16. **Gastric banding versus vertical banded gastroplasty:** We found one systematic review (search date 2001, 1 RCT)³⁵ and one subsequent RCT.³⁹ The RCT (59 adults with body mass index (see glossary, p 20) [BMI] ≥ 40 or BMI ≥ 37 with associated comorbidity) identified by the review found that people having gastric banding (see glossary, p 20) had smaller weight loss at 1 year compared with people having vertical banded gastroplasty (see glossary, p 20) (results not reported), but at 5 years people having gastric banding had lost more weight (43 kg with gastric banding v 35 kg with vertical banded gastroplasty; CI not reported).³⁵ The subsequent RCT (200 adults with BMI 40–50) found that significantly fewer people having gastric banding had an excellent or good result (defined as residual excess weight of $< 50\%$) at 2 years compared with people having vertical banded gastroplasty (35% with gastric banding v 74% with vertical banded gastroplasty; $P < 0.001$) Success rates were lower with gastric banding at 3 years, but the difference did not quite reach significance (25% with gastric banding v 63% with vertical banded gastroplasty; $P = 0.056$).³⁹

Harms: **Gastric banding versus gastric bypass:** See harms of gastric bypass, p 16. **Gastric banding versus vertical banded gastroplasty:** The first RCT reported one death from each group during the follow up period but neither death was attributed to the surgery. Re-operations occurred in 33% of people having vertical banded gastroplasty and 10% of people having gastric banding. Gastroesophageal reflux was more common in people having vertical banded gastroplasty compared with people having gastric banding (14.8% with gastroplasty v 11.5% with gastric banding).³⁵ No deaths were reported in the second RCT.³⁹ It found that gastric banding significantly increased the proportion of people who required re-operation compared with vertical banded gastroplasty (25% with gastric banding v 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 (33% with gastric banding v 14% with gastroplasty; $P < 0.001$).³⁹

Comment: None.

OPTION

GASTRIC BYPASS VERSUS OTHER BARIATRIC SURGICAL TECHNIQUES

RCTs provided moderate evidence that gastric bypass promoted greater weight loss than either gastroplasty or gastric banding. Five RCTs identified by a systematic review found that gastric bypass increased weight loss compared with horizontal gastroplasty. Two RCTs identified by the review found that gastric bypass increased weight loss at 1–3 years compared with vertical banded gastroplasty but another two RCTs found no significant difference between the procedures. One small RCT identified by the review found limited evidence of greater weight loss with gastric bypass than with gastric banding or vertical banded gastroplasty. Another small RCT identified by the review found that gastric bypass

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increased the proportion of people with 50% weight loss at 18 months compared with vertical banded gastroplasty or gastrogastrostomy. Perioperative mortalities were similar for these procedures. Postoperative complications were common and varied by type of procedure performed.

Benefits: We found one systematic review (search date 2001, 9 RCTs, 962 people) comparing gastric bypass (see glossary, p 20) versus vertical banded or horizontal gastroplasty (see glossary, p 20).³⁵ **Gastric bypass versus horizontal gastroplasty:** The review identified five RCTs (384 morbidly obese people) that compared gastric bypass versus horizontal gastroplasty.³⁵ All of the RCTs found that gastric bypass significantly increased weight loss compared with horizontal gastroplasty. Trials reported an average of 35–42% weight loss with gastric bypass compared with 16–29% with horizontal gastroplasty at 12 months ($P < 0.05$ in all RCTs). **Gastric bypass versus vertical banded gastroplasty, gastric banding, or gastrogastrostomy:** The review identified four RCTs that compared gastric bypass versus vertical banded gastroplasty and two RCTs that compared three interventions.³⁵ The first RCT (42 adults with body mass index (see glossary, p 20) ≥ 40) found that gastric bypass significantly increased weight loss compared with vertical banded gastroplasty at 12 months (percentage weight loss: 78% with gastric bypass v 52% with vertical banded gastroplasty; $P < 0.05$). The second RCT (40 adults > 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 (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; $P < 0.001$). The other two RCTs (109 adults, 32 with body mass index ≥ 40) found no significant difference in weight loss between the two procedures at 36 months, 3 years, and 5–6 years. The fifth RCT (77 adults) compared three interventions: gastric bypass, gastric banding (see glossary, p 20), or vertical banded gastroplasty. It found greater mean excess weight loss at 18 months with gastric bypass than with vertical banded gastroplasty or gastric banding (77% with gastric bypass v 65% with gastric banding v 60% with vertical banded gastroplasty; CI not reported). The sixth RCT (310 people) also compared three procedures: gastric bypass (99 adults), vertical banded gastroplasty (106 adults), or gastrogastrostomy (105 adults). It found that gastric bypass significantly increased the proportion of people who had a successful outcome (defined as 50% weight loss: 67% with gastric bypass v 48% with vertical banded gastroplasty v 17% with gastrogastrostomy; $P < 0.001$).³⁵

Harms: **Gastric bypass versus vertical banded gastroplasty:** Three RCTs comparing gastric bypass versus vertical banded gastroplasty identified by the review reported no deaths.³⁵ One RCT comparing gastric bypass versus vertical banded gastroplasty reported no deaths in the vertical banded gastroplasty group but two deaths (10%) in the gastric bypass group, occurring after 3 days and 12 months owing to presumed arrhythmia. **Gastric bypass versus horizontal gastroplasty:** Four RCTs comparing gastric bypass versus horizontal gastroplasty identified by the review reported no

operative mortality.³⁵ The fifth RCT reported two deaths: one 6 days after gastroplasty owing to anastomotic leak and cerebrovascular accident and one death within 30 days after gastric bypass owing to pulmonary embolism. The type of postoperative complications differed for these procedures. People having gastric bypass had symptomatic ulcer disease (25%), intractable vomiting and stomal stenosis (25%), marginal ulcers of jejunal side of gastrojejunostomy (5%), cholelithiasis (13%), and peptic gastroesophagitis (33%). People having vertical banded gastroplasty had superficial stomal erosions (5%), cholelithiasis (24%), and peptic gastroesophagitis (18%). One RCT found that significantly more people having gastric bypass had dumping syndrome (28% with gastric bypass v 0% with horizontal gastroplasty; $P < 0.05$) or heartburn (59% with gastric bypass v 32% with horizontal gastroplasty; $P < 0.05$). Other early and late complications varied little between procedures; however, one RCT reported that 32% of people having gastric bypass and 42% having gastroplasty had some form of postoperative complication.³⁵ **Gastric bypass versus gastric banding or vertical banded gastroplasty:** The RCT comparing gastric bypass, vertical banded gastroplasty, and gastric banding reported one death (group not specified).³⁵ One person who had vertical banded gastroplasty required re-operation (4%) for staple disruption, while 44% of people having gastric banding required re-operation for inadequate weight loss, nutritional disorder, or increased vomiting. **Gastric bypass versus vertical banded gastroplasty or gastrogastrostomy:** The RCT comparing gastric bypass, vertical banded gastroplasty, and gastrogastrostomy identified by the review reported two postoperative deaths (groups not specified), one from complications of a subsequent cholecystectomy, and one from carcinoma of the colon.³⁵ Early and late complication rates were similar among procedures.

Comment: Two systematic reviews were published after our search date, both of which concluded that gastric bypass results in greater weight loss than vertical banded gastroplasty.^{13,14}

OPTION GASTROPLASTY VERSUS OTHER BARIATRIC SURGICAL TECHNIQUES

Two RCTs found inconclusive results regarding weight loss with vertical banded gastroplasty compared with gastric banding. Five RCTs identified by a systematic review found that horizontal gastroplasty was less effective than gastric bypass for increasing weight loss. Four RCTs identified by the review found that vertical banded gastroplasty was less effective than gastric bypass in increasing weight loss at 1–3 years but another two RCTs found no significant difference between the procedures. Perioperative mortalities were similar for these procedures. Postoperative complications were common and varied by type of procedure performed. There is insufficient evidence to recommend one procedure over another.

Benefits: **Gastroplasty versus gastric banding:** See glossary, p 20. See benefits of gastric banding, p 15. **Gastroplasty versus gastric bypass:** See benefits of gastric bypass, p 16.

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Harms: **Gastroplasty versus gastric banding:** See harms of gastric banding, p 15. **Gastroplasty versus gastric bypass:** See harms of gastric bypass, p 16.

Comment: Two systematic reviews were published after our search date, and these reviews both concluded that vertical banded gastroplasty (see glossary, p 20) results in less weight loss than gastric bypass (see glossary, p 20).^{13,14}

OPTION BILIOPANCREATIC DIVERSION VERSUS OTHER BARIATRIC SURGICAL TECHNIQUES

Three systematic reviews identified no RCTs and we found no observational studies of sufficient quality comparing biliopancreatic diversion versus other bariatric procedures.

Benefits: We found three systematic reviews (search dates 2001,³⁵ 2003^{36,37}), which identified no RCTs comparing biliopancreatic diversion (see glossary, p 19) versus other bariatric surgery techniques.

Harms: We found no RCTs.

Comment: None.

OPTION OPEN VERSUS LAPAROSCOPIC BARIATRIC SURGERY

Five RCTs found no significant difference in weight loss between open and laparoscopic bariatric procedures. The RCTs found consistent evidence that laparoscopic surgery reduced the incidence of wound and incisional hernia complications compared with open surgery. They found more limited evidence that laparoscopic procedures decreased length of hospital stay compared with open procedures; data are insufficient to draw conclusions about other complication rates.

Benefits: We found one systematic review (search date 2001, 3 RCTs, 256 people with morbid obesity)³⁵ and two subsequent RCTs^{40,41} comparing open versus laparoscopic techniques. **Open versus laparoscopic gastric banding:** The review identified one RCT (50 adults with body mass index (see glossary, p 20) ≥ 40) that found no significant difference in weight loss between open and laparoscopic gastric banding (see glossary, p 20) at 12 months (34.4 kg with open v 35.0 kg with laparoscopic; P reported as non-significant).³⁵ **Open versus laparoscopic gastric bypass:** The review identified two RCTs and we found one subsequent RCT that found no significant difference in weight loss at 1 and 2 years between open and laparoscopic gastric bypass (see glossary, p 20).^{35,40} The first RCT (155 people) identified by the review found no significant difference in weight loss at 1 year (62% with open v 68% with laparoscopic; P = 0.07). The second RCT (51 people) identified by the review also found no significant difference in body mass index (BMI) at 1 year (reduction in BMI: 13 kg/m² with open v 14 kg/m² with laparoscopic; reported as non-significant, CI not reported in review). The subsequent RCT (104 people with morbid obesity) found no significant difference in weight loss at a mean 23 months between open and laparoscopic techniques (reported as non-significant, results presented graphically).⁴⁰ **Open versus laparoscopic vertical**

banded gastroplasty: The review identified no RCTs.³⁵ One subsequent RCT (30 adults with body mass index 40–50) found similar weight loss between open and laparoscopic vertical banded gastroplasty (see glossary, p 20) at 12 months (mean: 55% with open v 47% with laparoscopic; CI not reported).⁴¹

Harms:

Open versus laparoscopic gastric banding: One of the RCTs reported no deaths.³⁵ The review found no significant difference in surgical complications between the two procedures (reported as non-significant, CI not reported in the review), although people having open gastric banding had more incisional hernia complications (12% with open v 0% with laparoscopic). Re-admissions and overall length of hospital stay were significantly higher in people having open compared with laparoscopic procedures (re-admissions: 60% with open v 24% with laparoscopic; hospital stay: 11.8 days with open v 7.8 days with laparoscopic; $P < 0.05$ for both outcomes). **Open versus laparoscopic gastric bypass:** The RCTs reported four postoperative deaths: one owing to malignant hyperthermia, one owing to possible pulmonary thromboembolism (laparoscopic), one owing to intestinal obstruction (laparoscopic), and one owing to evisceration.^{35,40} The review found no significant difference between open and laparoscopic bypass in the proportion of people who had major surgical complications (9.2% of people with open v 7.6% of people with laparoscopic; $P = 0.78$).³⁵ In all three RCTs identified by the review, minor complications (including vomiting, colicky pain, and wound infection) were not significantly different between groups.³⁵ The subsequent 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 bypass (24% with open v 11% with laparoscopic; $P < 0.05$).⁴⁰ Operating time was longer for the laparoscopic procedure in two RCTs and longer for the open procedure in one RCT. Hospital stay was significantly shorter for the laparoscopic procedure in all three RCTs (4–8 days with open v 3–5 days with laparoscopic; $P < 0.05$). **Open versus laparoscopic vertical banded gastroplasty:** The RCT reported no deaths.⁴¹ Operating time was significantly longer for the laparoscopic procedure (2.10 hours with open v 1.45 hours with laparoscopic; $P = 0.002$), but average hospital stay was not significantly different (4 days for both techniques). Two people, one in each group, developed a fistula at the gastric partition that required re-operation. Two people having open gastroplasty (see glossary, p 20) developed abdominal wall hernias at 12 months.

Comment:

One systematic review was published after our search date, which also concluded that laparoscopic procedures result in fewer wound complications or incisional hernias than open procedures.¹⁴

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 a 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

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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.

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

Extrapyramidal effects Include acute dystonia, a Parkinsonism-like syndrome, and akathisia.

Gastric banding involves placing an adjustable band around the upper portion of the stomach. The band is connected to a reservoir, which the surgeon can tighten or loosen, by the infusion of varying amounts of a saline solution. The newly created upper pouch will only allow the person to consume small amounts of food at a time.

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 “bypassed” 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 gastrointestinal 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 which 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.

Serotonin syndrome Clinical features include agitation, ataxia, diaphoresis, diarrhoea, fever, hyper-reflexia, myoclonus, shivering, and changes in mental status. The occurrence and severity of syndrome does not seem to be dose related.

Substantive changes

Sibutramine One systematic review¹⁷ and one subsequent RCT added;¹⁸ categorisation unchanged.

Orlistat One systematic review³² and one subsequent RCT added;³³ categorisation unchanged.

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