BARIATRIC SURGERY

Rapid Evidence Review: 'Which clinical criteria are associated with the most cost effective use of tier 4 bariatric services?'

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Changes made to revised RER

Page	Section	Original Text	Revised Text
1	Context	between 35 kg/m^2 and 35.9 kg/m^2	between 35 kg/m^2 and 40 kg/m^2
2	Cost Effectiveness	BMI of 35 kg/m^2 to 34.9 kg/m^2	BMI of 35 kg/m^2 to 40 kg/m^2
3	Cost Effectiveness	The reported ICERs	The reported incremental cost effectiveness ratios (ICERs)
21	Schauer 2017	a parallel randomised controlled trial	a parallel randomised controlled trial (the STAMPEDE study)
25	Type 2 diabetes	the remission rate of type 2 diabetes was statistically significantly higher in participants receiving LAGB after two years	the remission rate of type 2 diabetes was statistically significantly higher after two years in participants receiving LAGB
32	Cost Effectiveness	bariatric surgery in general is cost effective, particularly LRYGB and LAGB, which were both approximately US$5,000 6,000 per QALY	bariatric surgery in general is cost effective, particularly LRYGB and LAGB, which were both approximately US$5,000 to US$6,000 per QALY

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Questions to be addressed

The aim of this rapid evidence review is to understand the evidence which will answer the question:

'Which clinical criteria are associated with the most cost effective use of tier 4 bariatric services?'

In order to develop an effective search strategy to find the relevant evidence that will answer this question, two detailed sub-questions were developed:

a) In adults with obesity (BMI at least 35 kg/m^2) with or without associated co-morbidities what is the clinical and cost effectiveness of bariatric surgery compared with non-surgical management?

b) Are there any sub-groups who would benefit more from bariatric surgery than others (defined by, for example, initial BMI status and/or presence of a specific co-morbidity)?

Summary of Evidence

Context

- The risk of developing obesity-related co-morbidities increases as an individual's Body Mass Index (BMI) increases.
- The NICE clinical guideline (CG189) recommends that bariatric surgery should be considered for all patients with a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 and other significant disease.
- In the UK, the surgical procedures most commonly used are adjustable gastric banding, sleeve gastrectomy and Roux-en-Y gastric bypass.
- NHS England has transferred commissioning responsibility for tier 4 services to Clinical Commissioning Groups from April 1st 2016. In order to achieve a smooth transition during 2016/17, NHS England continued to negotiate and contract activity whilst CCGs built relationships and planned pathways.
- The information in this review supports evidence based commissioning and planning of weight management pathways for 2017/18.

Clinical Effectiveness

- There was a lack of high-quality randomised controlled trials and trials with long-term follow-up.
- The evidence base covers a wide variety of different non-surgical interventions, making direct comparison difficult due to study heterogeneity.
- A Cochrane systematic review found greater weight loss following bariatric surgery for follow-up periods of one to two years when compared to non-surgical interventions.

- There is good quality evidence that bariatric surgery reduces, but does not eliminate the risk of developing diabetes.
- A large, good **quality** study based on the Clinical Practice Research Datalink found that 4.3% of bariatric surgery patients had developed diabetes after seven years, compared to 16.2% of controls.
- There is moderate quality evidence that bariatric surgery reduces metabolic syndrome and weak evidence for improvement in sleep apnoea, however evidence for the benefits relating to hypertension and lipid profiles was inconsistent.

Safety

- The UK National Bariatric Surgery Registry reports that bariatric surgery in the UK is considered safe, with a mortality rate of around one in 1,000.
- Evidence relating to patient safety was generally poor due to inconsistent reporting, different reporting methods between studies and the small number of incidents.
- The short-term follow-up time of studies precludes the possibility of directly comparing the safety of surgery against non-surgical interventions, where individuals not achieving significant weight loss may live with co-morbidities for extended periods of time.

Cost Effectiveness

- There is moderate quality evidence to suggest that bariatric surgery is highly cost effective (less than £20,000 / QALY over a lifetime).
- Cost effectiveness is highly dependent upon the co-morbidity costs avoided, either through remission of existing co-morbidities or a reduction in the risk of developing obesity related co-morbidities in the future.
- Bariatric surgery is highly cost effective for individuals with a BMI 40 kg/m^2 or more and also for those with a BMI of 35 kg/m^2 to 40 kg/m^2 and a significant co-morbidity.
- Bariatric surgery was found to be particularly cost effective for individuals with a BMI of 40 kg/m^2 or more and type 2 diabetes.
- Bariatric surgery is likely to be most cost effective in patients with the most capacity to benefit: younger patients; or those with a higher BMI; or those with an existing obesity-related co-morbidity which is likely to be resolved by significant weight loss resulting from bariatric surgery.

Questions

a. In adults with obesity (BMI at least 35 kg/m^2) with or without associated co-morbidities what is the clinical and cost effectiveness of bariatric surgery compared with non-surgical management?

Clinical effectiveness

Bariatric surgery was found to consistently achieve greater weight-loss than non-surgical interventions.

There is moderate quality evidence that bariatric surgery results in greater weight loss for follow-up periods of one to two years, regardless of the surgical procedure or type of participants included. Weight loss is associated with a reduction in co-morbidities such as type 2 diabetes, metabolic syndrome and sleep apnoea but benefits relating to hypertension and lipid profiles are inconsistent.

Those who do manage to achieve weight loss without surgery are likely to regain weight in the future.

A good quality trial based on Clinical Practice Research Datalink records reported that it was difficult to achieve normal body weight or even just a 5% reduction in initial body weight without surgery. Only a small proportion of individuals who achieve a modest reduction in weight without surgery manage to avoid weight regain two to five years later.

The observed evidence falls in favour of surgical interventions for weight loss and resolution of co-morbidities (particularly type 2 diabetes), It would seem reasonable to conclude that the provision of lifestyle interventions is less clinically effective at dealing with more severe levels of obesity. The risks and benefits of surgery need to be carefully considered given the poor quality of information available in the literature pertaining to patient safety; however, the data provided by the Bariatric Surgery Register goes some way toward countering these concerns.

Cost effectiveness

All of the studies included clearly indicate that bariatric surgery (particularly if performed laparoscopically which is current UK clinical practice) is highly cost effective against both the NICE 'usual' cost effectiveness threshold of £20,000 to £30,000 per QALY, and the 'affordable' NHS threshold estimated by Karl Claxton et al of circa £12,000 per QALY. The reported incremental cost effectiveness ratios (ICERs) are consistently lower than the £20,000 per QALY ceiling by a factor of between four and ten (depending on the estimate considered).

For a mixed population (with and without co-morbidities), there are reliable and authoritative estimates of the lifetime ICER from the recently published UK NIHR cohort study and cost effectiveness analysis by Gulliford et al (2016). Over a lifetime, bariatric surgery resulted in both additional QALYs and was highly cost effective with an ICER of £7129 (95%CI £6775 to £7506) per QALY. The ICER for patients with severe obesity alone was slightly higher but, at £7675 per QALY, it was still well within UK accepted norms. The authors found that bariatric surgery was particularly cost effective in patients with morbid obesity and type 2 diabetes mellitus (T2DM) (£6176 per QALY).

The NIHR report did not find bariatric surgery to be cost saving over the lifetime but this may be because this model included a wider range of costs directly associated with the bariatric surgery pathway as well as a more realistic estimate of diabetes remission and recidivism.

Consistent with these findings, there is evidence from the UK HTA evaluation that bariatric surgery is also highly cost effective over a shorter, 20 year time horizon both for patients with a BMI of more than 40 kg/m^2 and no co-morbidity (ICER less than £5000 per QALY), as well as for patients with a BMI of more than 35 kg/m^2 and T2DM (£1634 per QALY).

b. Are there any sub-groups who would benefit more from bariatric surgery than others (defined by, for example, initial BMI status and/or presence of a specific co-morbidity)?

Individuals with type 2 diabetes who received surgery experienced higher rates of remission than those receiving non-surgical interventions.

Good quality evidence was identified reporting that bariatric surgery resulted in significantly higher remission rates for type 2 diabetes compared to non-surgical interventions.

As noted by NICE in its guidance for preventing ill health and premature death in black, Asian and other minority ethnic groups, these groups are at an equivalent risk of diabetes, other health conditions or mortality at a lower BMI than the white European population. Because of this, it may prove prudent to examine the possibility of providing weight loss interventions to these groups at a lower threshold BMI value than is currently used for the general population.

Cost effectiveness is highly dependent on the avoidance of healthcare costs associated with co-morbidities. These costs may be avoided either from remission (temporary or otherwise) or avoidance of future incidence of obesity-related co-morbidity.

Patients with the greatest capacity to benefit are likely to be the most cost effective group to treat.

From an economic perspective, bariatric surgery is likely to be most cost effective in patients who are:

- Younger or
- Have a higher BMI or
- Have an existing obesity-related co-morbidity which is likely to be resolved by significant weight loss resulting from bariatric surgery.

Options for commissioners

- To continue to commission bariatric surgery procedures for patients who meet the current NICE eligibility criteria (a BMI of 40 kg /m^2 or more or between 35 kg /m^2 and 40 kg /m^2 and other significant disease).
- To continue to commission bariatric surgery procedures for patients who meet the current NICE eligibility criteria (a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 and other significant disease) with priority given to patients based on likely capacity to benefit (e.g. younger patients, patients in whom surgery is likely to prevent or resolve obesity-related co-morbidities, such as type 2 diabetes, sleep apnoea or metabolic syndrome, or those whose weight is such that surgery will achieve improvements in health relatively quickly).
- In addition to points one and two, commissioners may also opt to extend the BMI threshold for surgery for certain ethnic groups who present with higher risk at lower BMI levels, as recommended by NICE.

1 Context

This rapid evidence review is an update of a full review undertaken in July 2016 when a search for evidence back to 2006 was undertaken. The search for this update is therefore from July 2016 to June 22nd 2017.

1.1 Introduction

Obesity is commonly defined as a Body Mass Index (BMI) of 30 kg/m^2 or greater (see Table 1). Individuals living with obesity are at greater risk of a variety of different health conditions. These include type 2 diabetes mellitus (T2DM), non-alcoholic fatty liver disease, hypertension, asthma, gastro-oesophageal reflux disease, depression and a variety of other conditions [1]. The risk of developing obesity-related co-morbidities increases as an individual's BMI increases [2].

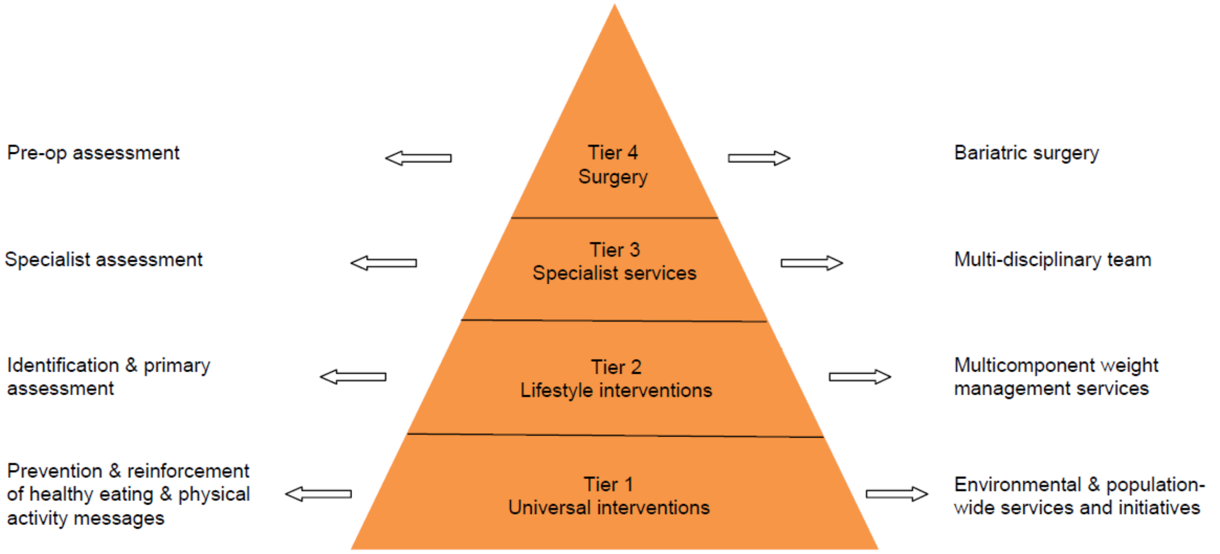
Table 1: NICE BMI Categories

Definition	BMI range (kg/m^2)
Underweight	Under 18.5
Normal	18.5 to less than 25
Overweight	25 to less than 30
Obese	30 to less than 40
Obese I	30 to less than 35
Obese II	35 to less than 40
Morbidly obese	40 and over

Source: NICE. Obesity: identification, assessment and management [1]

In England, obesity is managed through a tiered system (Figure 1), ranging from preventive population-based health promotion strategies (Tier 1) and lifestyle interventions (including diet, exercise, and behavioural) in primary care settings (Tier 2), through to more intensive specialist services provided by multi-disciplinary teams (tier 3) and bariatric surgery (tier 4) [3].

Figure 1: Tiered management of obesity



Source: Department of Health. Developing a specification for lifestyle weight management services. 2013 [3]

1.2 Existing national policies and guidance

In November 2014, NICE published clinical guidance on the identification, assessment and management of obesity (NICE clinical guideline 189), replacing the older section 1.2 in 'Obesity' (NICE clinical guideline 43) [1].

According to the NICE Obesity pathway (Figure 2): "*Bariatric surgery is a treatment option for people with obesity if all of the following criteria are fulfilled:*

- *They have a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 and co-morbidity (for example, type 2 diabetes or high blood pressure) that could be improved if they lost weight*
- *All appropriate non-surgical measures have been tried but the person has not achieved or maintained adequate, clinically beneficial weight loss*
- *The person has been receiving or will receive intensive management in a tier 3 service*
- *The person is generally fit for anaesthesia and surgery*
- *The person commits to the need for long-term follow-up*"

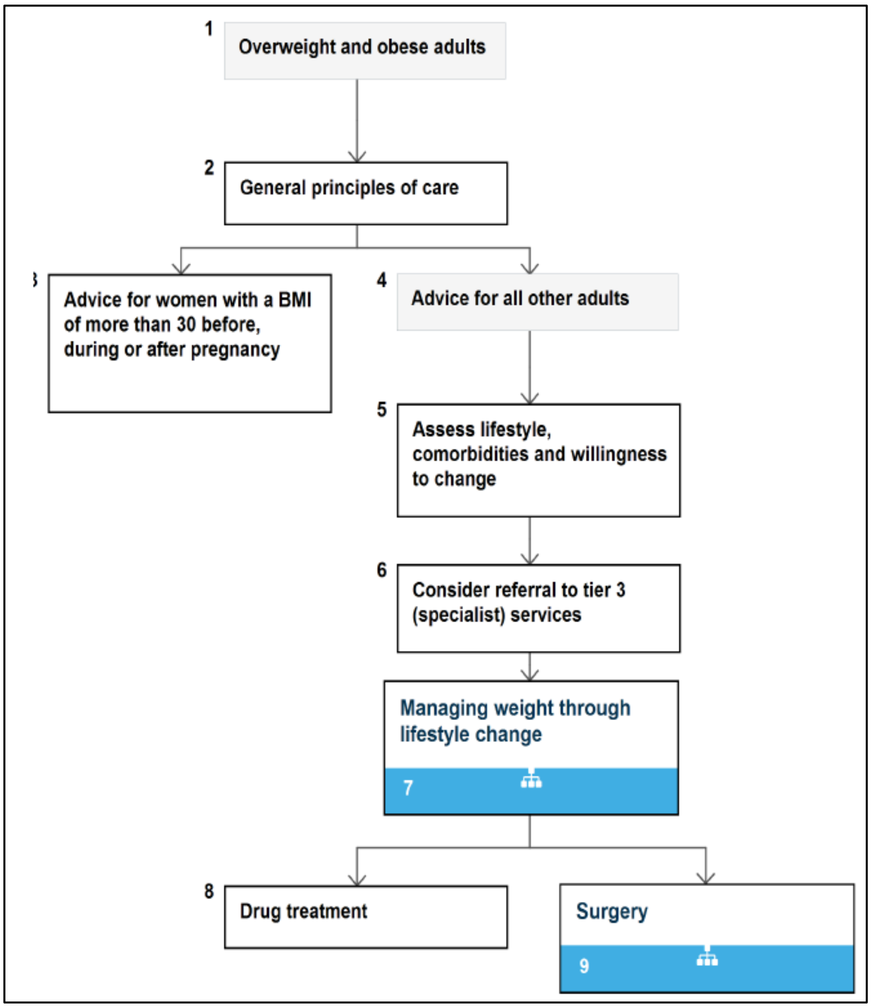
In addition to the criteria listed above, bariatric surgery is the option of choice (instead of lifestyle interventions or drug treatment) for adults with a BMI of more than 50 kg/m^2 when other interventions have not been effective.

To support commissioning of bariatric surgery services, NICE has published a costing template that enables commissioners to complete an economic modelling exercise to assist with decision-making on the thresholds at which this service will be offered [4].

NICE has also published guidance on the following surgical procedures:

- Implantation of a duodenal-jejunal bypass sleeve for managing obesity, which should only be used in the context of research [5]
- Laparoscopic gastric plication for the treatment of severe obesity, with special arrangements for clinical governance, consent and audit or research [6].

Figure 2: NICE pathway for overweight and obese adults



Source: NICE. Overweight and obese adults - NICE Pathways [7]

1.2.1 Non-Surgical Interventions

The commissioning of tier 3 obesity services is a local consideration, aimed at those individuals with either a BMI of 40 kg/m^2 or more or those with a BMI of 35 kg/m^2 or more and an additional co-morbidity. The provision of tier 3 services is variable and indeed absent in many areas [8]. In a recent mapping exercise lead by Public Health England, it was found that 13% of local authorities who responded to a survey commissioned a tier 3 service [9]. Services were primarily split between healthcare settings (GP surgery or hospital, n=21) and community/leisure centre settings (n=20). Programmes tended to be delivered on a one-to-one basis, with referrals originating from GPs, practice nurses or other health professionals. Follow up was reported to last for twelve months or longer.

NICE has published guidance which describes the constituent components of non-surgical weight-management interventions. NICE recommends that programmes are multi-component and address the following areas:

- Behavioural interventions
- Physical activity
- Dietary
- Pharmacological interventions [1].

In addition to this, NICE's public health guidance 'Weight management: lifestyle services for overweight or obese adults' recommends that commissioners ensure that weight management services are multi-component and lead by a multidisciplinary team [10].

According to the NICE obesity pathway (Managing weight through lifestyle change in adults), treatments should be selected based on individual preference, social circumstance and the outcomes of previous interventions. In addition, the individual's level of risk based on BMI, waist circumference and the presence of co-morbidities should be taken into account (see Table 2). The level of intervention should be higher for those with co-morbidities, regardless of waist circumference [11]. NICE also recommends that lower BMI thresholds should be used with black, Asian and other minority ethnic group populations due to the heightened risk of developing type 2 diabetes amongst these groups [12].

In its current form, tier 3 services are often seen as a bridging service prior to patients entering tier 4. In some instances it may even be seen as merely an intermediary step in preparing patients for bariatric surgery [13].

Table 2: NICE Obesity Intervention Risk Matrix

BMI classification	Waist circumference			Comorbidities present
	Low	High	Very high	
Overweight	1	2	2	3
Obesity I	2	2	2	3
Obesity II	3	3	3	4
Obesity III	4	4	4	4

1 = General advice on healthy weight and lifestyle

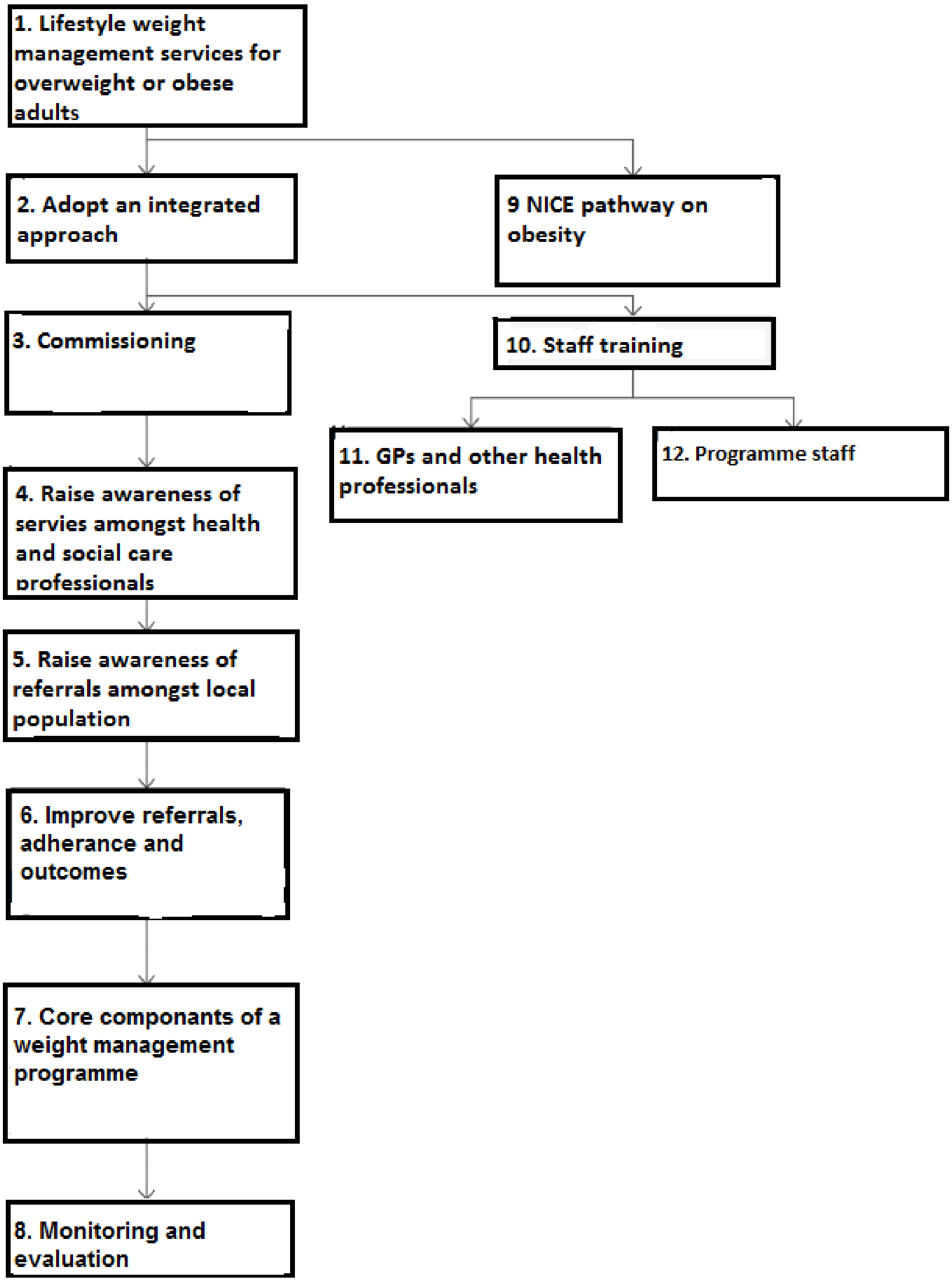
2 = Diet and physical activity

3 = Diet and physical activity; consider drugs

4 = Diet and physical activity; consider drugs; consider surgery

Source: NICE. Managing weight through lifestyle change in adults - NICE Pathways [11]

Figure 3: NICE pathway for managing weight through lifestyle change



Source: NICE. Managing weight through lifestyle change in adults - NICE Pathways [11]

2 Epidemiology

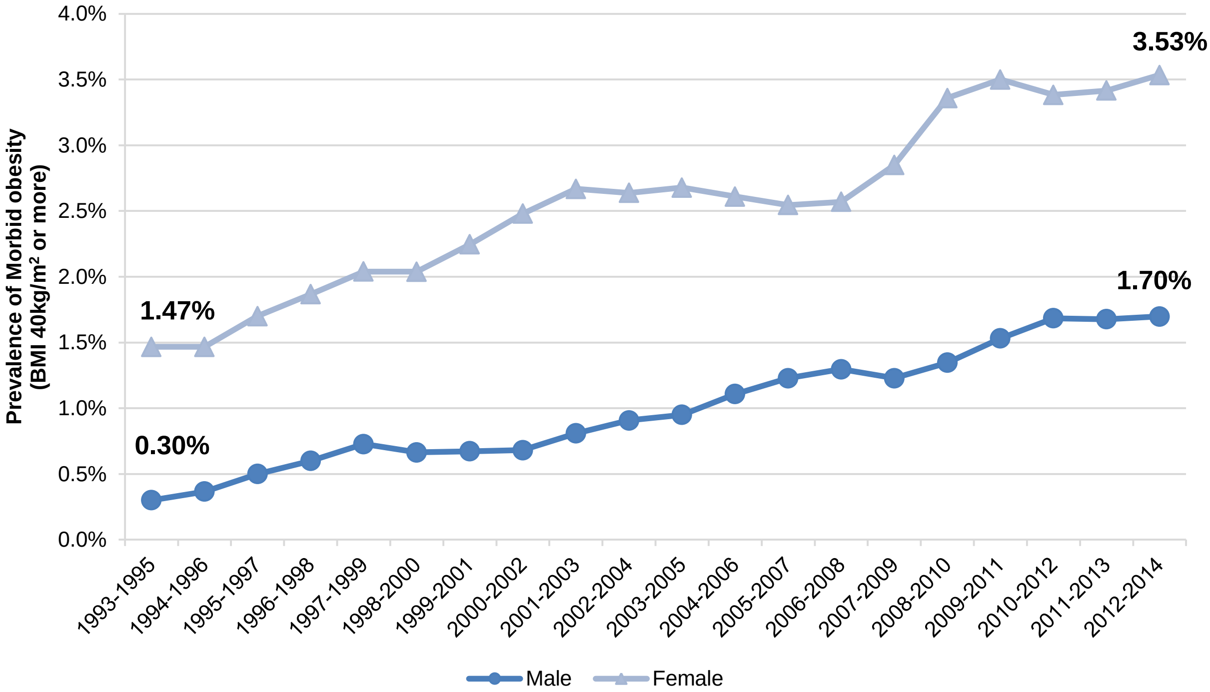
2.1 Obesity

Obesity is a global problem, estimated to have affected over six hundred million adults worldwide in 2014 [14]. In England, in both men and women, more than one in four adults are obese (28.2%) and 2.7% are classed as morbidly obese [15].

The prevalence of obesity in the UK rose between 1993 and 2014, the rate of increase began to slow in 2001 but the overall trend is still continuing to rise. According to the Health Survey for England, 61.7% of adults were overweight or obese in 2014, with more men being obese (65.3%) than women (58.1%) [16, 17]. Over the same time period, the prevalence of morbid obesity has also continued to climb, with a sharp rise in female prevalence between 2007 and 2011 (see Figure 4). Whilst the trend for males appears to have levelled off in recent years, the current level still represents a sizeable increase from that seen in the early 1990's. The number of people classed as obese in the UK is expected to increase by 11 million by 2030, with a likely corresponding increase in those with morbid obesity [18].

According to forecasts produced by the World Health Organisation, 31% of men and 30% of women will be obese by 2020, rising to 36% and 33% respectively by 2030 [19].

Figure 4: Trend in prevalence of morbid obesity among adults in UK from 1993-1995 to 2012-2014 (3 year rolling average)



Source: Health and Social Care Information Centre. Health Survey for England, 2014 [16]

2.2 Co-Morbidities

The health issues associated with being overweight or obese include type 2 diabetes mellitus, cardiovascular disease and musculoskeletal disorders amongst others. People aged 35 to 59 with a BMI measurement of between 40 kg/m^2 and 50 kg/m^2 are five times more likely to die from ischaemic heart disease than those with a BMI of 22.5 kg/m^2 to 25 kg/m^2. Between the same groups, the risk of dying from stroke was 6.5 times higher and the risk of dying from diabetes was 22.5 times higher. Vascular risk factors also exhibit a strong relationship with BMI; both systolic and diastolic blood pressure increases with BMI [20].

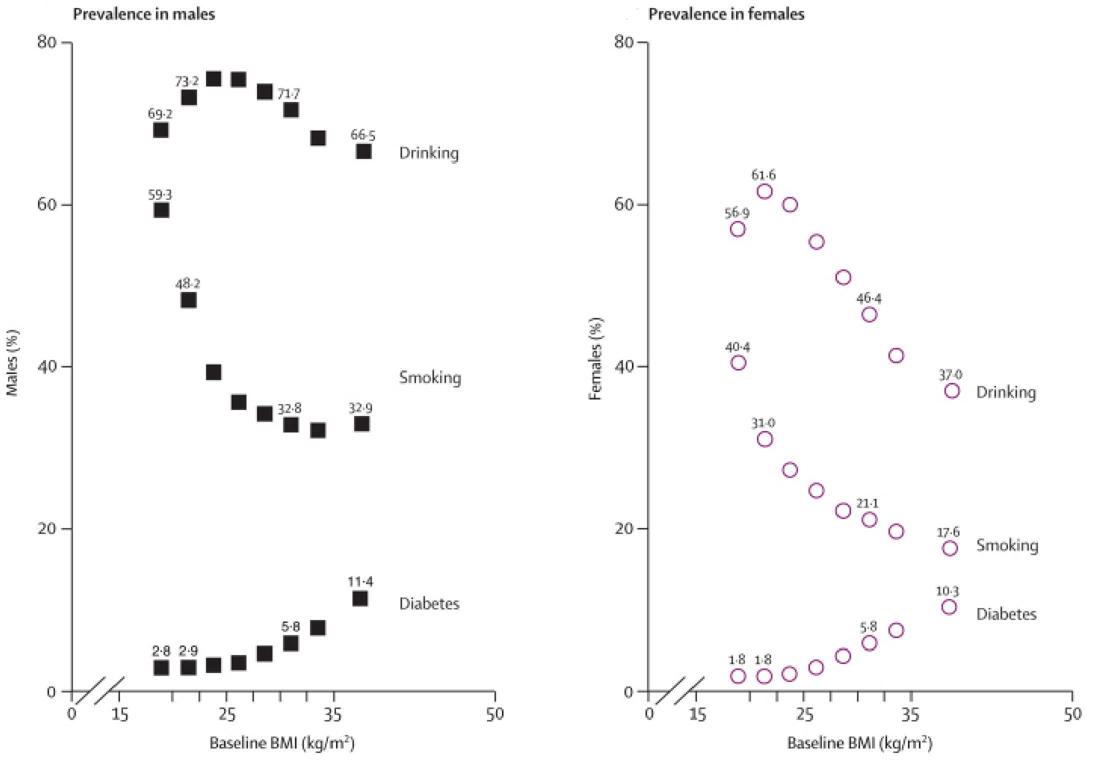
The prevalence of diabetes amongst those with normal weight was around 1.5%, compared to 15% in the severely obese [20]. A table showing the simplified relationship between BMI and health risk is shown below (Table 3). On its own, BMI is a strong predictor of mortality and is strongly associated with diabetes for which sex-specific prevalence may rise more than five-fold from baseline across the BMI range (see Figure 5) [21].

Table 3: Co-Morbidity Risk by BMI Classification

Classification	BMI (kg/m^2)	Risk of Obesity Related Co-Morbidities
Underweight	<18.5	Low risk (but risk of other clinical problems increased)
Normal Range	18.50 – 24.99	Average risk
Overweight	≥25.0	Increased risk
Obese	≥30.0	Medium to high risk
Morbidly Obese	≥40.0	Very high risk

Source: Public Health England Obesity Knowledge and Intelligence team. Severe Obesity [20]

Figure 5: Changes in prevalence of risk factors (drinking, smoking and diabetes) in males and females according to baseline BMI in the range 15–50 kg/m^2



Source: Prospective Studies Collaboration. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. Lancet 2009;373 (9669):1083–96 [21].

3 The Intervention

3.1 Bariatric Surgery

Bariatric surgery includes a group of procedures that promote weight loss. They are usually performed laparoscopically, with decreased time in hospital and a shorter recovery time compared to open procedures. In the UK and Ireland, there were over 18,000 bariatric surgery operations in the three financial years ending 2011, 2012, and 2013; 95.4% of all primary operations were performed laparoscopically over this period [22]. More recently, minimally invasive surgical techniques also include robotic procedures, though their feasibility and safety are debated. Bariatric surgery may be categorised under three headings: restrictive; malabsorptive and combined procedures.

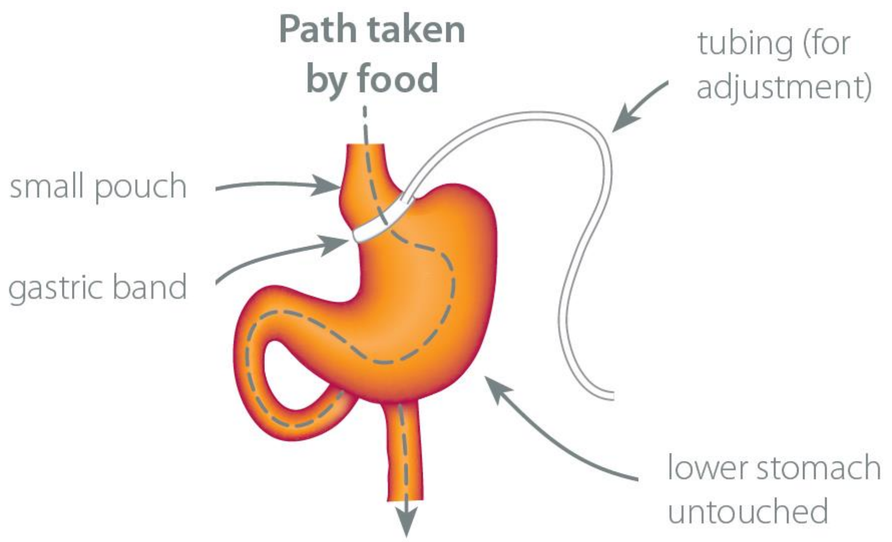
3.1.1 Restrictive procedures

Restrictive procedures, described below, lead to a fixed or adjustable reduction in the size of the upper gastrointestinal tract.

Adjustable gastric banding (AGB)

This procedure places an adjustable silicone band around the upper stomach, creating a small pouch above the band and a narrowing between the pouch and main part of the stomach below it (Figure 6). This restricts the amount of food that can be eaten and reduces hunger sensations by pressing on the surface of the stomach. The band may be tightened or loosened by injecting or removing saline through a portal under the skin that is connected to the band. The procedure is reversible and relatively non-invasive. AGB has replaced the older restrictive gastroplasty (horizontal, vertical, and banded) procedures that are no longer performed in the UK due to poorer performance. Gastric banding made up 22.3% of all bariatric surgery operations in the UK between 2011 and 2013 [22, 23, 24].

Figure 6: Diagrammatic representation of a gastric band in place

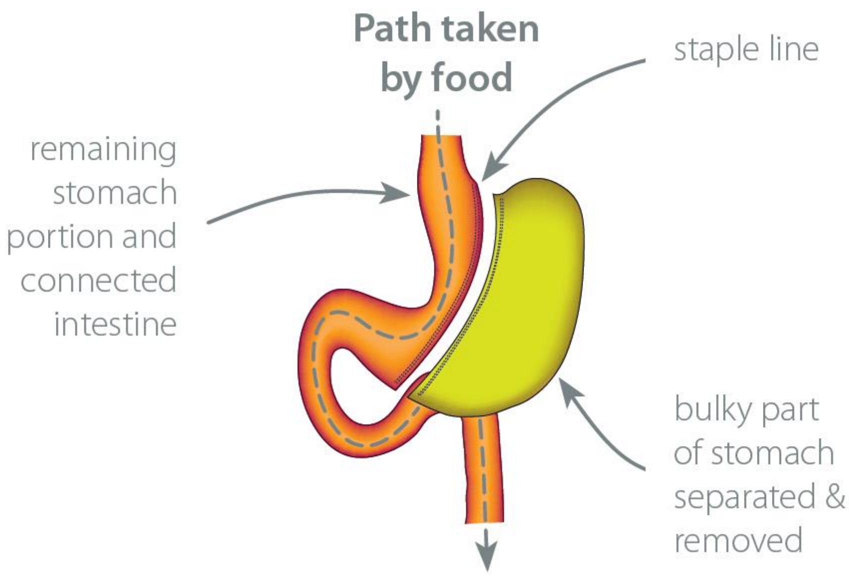


Source: National Bariatric Surgery Register. NSBR Second Registry Report. 2014 [22]

Sleeve gastrectomy (SG)

This procedure divides the stomach vertically to reduce its size by seventy-five percent, whilst keeping the stomach function and digestion unaltered by leaving the pyloric valve intact (see Figure 7). The procedure is not reversible, but is relatively quick to perform and is one of the most commonly performed restrictive procedures. It was initially used as the first of a two-part procedure for patients at high risk from bariatric surgery, followed by a conversion to either a Roux-en-Y gastric bypass or a duodenal switch (see below). However, as some patients achieve significant weight loss with the sleeve gastrectomy alone, it is now also used as a stand-alone procedure. In some patients, the procedure may be followed by a duodenojejunal bypass, which involves bypassing the first part of the small intestine, resulting in food moving directly to the latter part of the small intestine, thereby reducing absorption of calories. SG made up 20.8% of all bariatric surgery operations in the UK between 2011 and 2013 [22]. A further 12 (0.07%) SG procedures were performed in combination with a biliopancreatic diversion with duodenal switch [22].

Figure 7: The basics of a sleeve gastrectomy procedure



Source: National Bariatric Surgery Register. NSBR Second Registry Report. 2014 [22]

Intragastric balloon (IGB)

Intragastric balloon procedures involve placing a silicon balloon endoscopically to float freely inside the stomach, thereby reducing the volume of the stomach, leading to an earlier sensation of satiety. It is typically used either in patients who are at least 40% of their optimal weight, or in morbidly obese patients for whom surgery is high risk. IGB made up 2.1% of all bariatric surgery operations in the UK between 2011 and 2013 [22].

Gastric plication (or gastric imbrication)

A newer procedure that reduces the stomach volume by folding the stomach into itself and stitching it to create a narrow tube shape, similar to that of SG, but without removing any stomach tissue (Figure 6). The Registry report does not present the exact number or proportion of all bariatric surgery operations that involve gastric plication. However, it is less than the 2.1% procedures labelled as ‘other’ in the Registry report [22].

3.1.2 Malabsorptive procedures

Malabsorptive procedures bypass a section of the intestine, with less physical restriction of food intake.

Biliopancreatic diversion (without duodenal switch)

This procedure is typically no longer performed in the UK due to risk of postgastrectomy syndrome (including, for example, dumping syndrome, bile reflux, diarrhoea). It involved portions of the stomach being removed through a horizontal gastrectomy (a restrictive procedure), with the small remaining pouch being connected to the final section of the small intestine. This is now replaced with the biliopancreatic diversion with duodenal switch (BDDS) procedure, which may be classed as a combined procedure (see group 3 below).

Jejunoileal bypass (JIB)

This procedure is no longer performed in the UK, where a significant part of the small intestine was detached and set to the side.

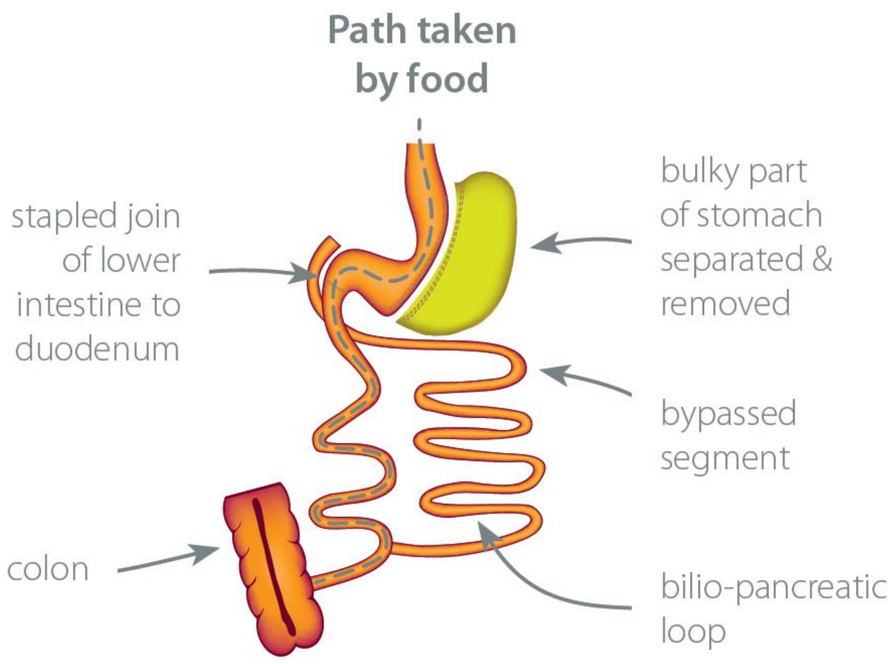
3.1.3 Combined procedures

Combined procedures include both restrictive and malabsorptive components.

Biliopancreatic diversion with duodenal switch (BDDS)

Biliopancreatic diversion with duodenal switch involves an initial restrictive vertical gastrectomy, followed by the malabsorptive component which re-routes a long portion of the small intestine, creating two separate pathways and one common channel (Figure 8). The shorter of the two pathways, the digestive loop, takes food from the stomach to the common channel. The longer pathway, the biliopancreatic loop, carries bile from the liver to the common channel. This procedure reduces the amount of time the body has to capture calories from food in the small intestine, and selectively limits the absorption of fat. The procedure is partially reversible, but there were only 19 BDDS procedures (0.1%), together with a further 12 procedures combined with SG in the UK between 2011 and 2013 [22].

Figure 8: Biliopancreatic diversion with duodenal switch

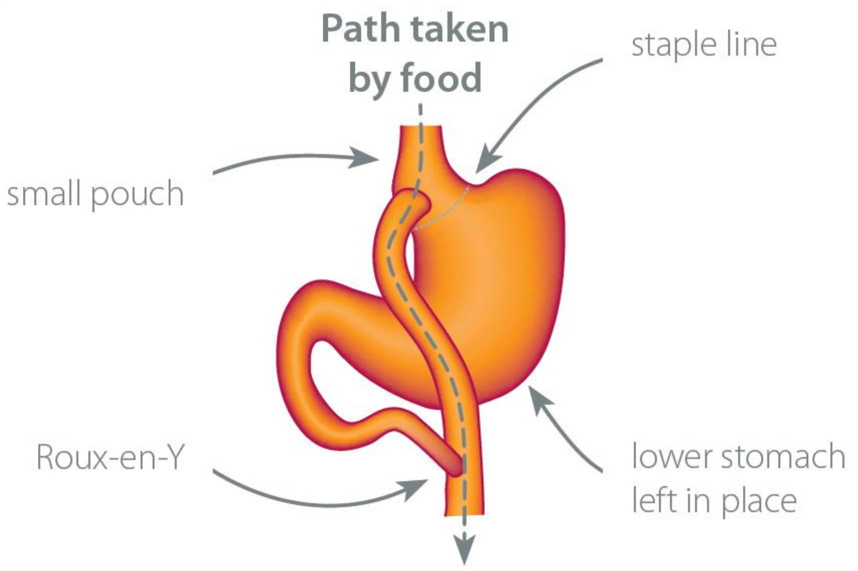


Source: National Bariatric Surgery Register. NSBR Second Registry Report. 2014 [22]

Roux-en-Y gastric bypass (RYGB)

Roux-en-Y gastric bypass has replaced the older banded gastric bypass, and involves creating a small pouch from the stomach which remains attached to the oesophagus at one end, and connected to a section of the small intestine at the other end, thereby bypassing the remaining stomach and the initial loop of small intestine (Figure 9). This procedure reduces intestinal absorption. Adaptations of the procedure have been used to increase malabsorption and increase weight loss. The procedure is technically reversible. Roux en Y gastric bypass comprises 52.1% of bariatric surgery in the United Kingdom [22].

Figure 9: Diagrammatic representation of a Roux-en-Y gastric bypass procedure



Source: National Bariatric Surgery Register. NSBR Second Registry Report. 2014 [22].

3.2 Non-Surgical Interventions

Non-surgical interventions for obesity consist of a wide variety of measures which may be used in varying combinations as part of a multi-component pathway. Generally this comprises dietary intake, physical activity levels and behaviour change and may also include pharmacological interventions [25]. These should be clinically lead and involve multi-disciplinary assessment [13].

In 2014 the Royal College of Surgeons and the British Obesity and Metabolic Surgery Society released commissioning guidance pertaining to tier 3 weight assessments and management clinics [13]. This provides thresholds for GPs referring into a tier 3 service (see Table 3), though it should be noted from the report that these BMI thresholds were chosen purely due to them matching classifications commonly used in research literature:

"The current BMI thresholds for surgery were chosen arbitrarily as the criteria for referral into the clinic since the quoted literature predominantly refers to patients in these groups."

Table 3: Referral Thresholds for tier 3 Services

BMI (kg/m^2)	Co-Morbidity	Comment
≥40	None	
≥35 to <40	Type 2 Diabetes	May be reduced by 2.5 kg/m^2 in Asians
≥35 to <40	Obesity related co-morbidity (e.g. metabolic syndrome, hypertension, obstructive sleep apnoea, depression etc.)	Occasionally patients may be referred who do not meet these thresholds, such as those presenting with weight regain post bariatric surgery

The tier 3 service should be provided via a multidisciplinary team containing a bariatric physician, dietitian, specialist nurse, clinical psychologist and a liaison psychiatry professional. In addition to this there should also be access to a physical therapist.

Non-surgical weight-management interventions (also known as 'Lifestyle Interventions') are commonly split into four categories:

1. Behavioural interventions
2. Physical activity
3. Behaviour change
4. Pharmacological interventions.

Interventions should be seen as multicomponent and incorporate combinations of the interventions described below.

3.2.1 Behavioural interventions

Behavioural interventions are provided with the support of an appropriately trained professional and include various strategies for adults which are incorporated as appropriate. These include (but are not limited to) self-monitoring of behaviour and progress, stimulus control, goal setting, ensuring social support is available, cognitive restructuring (modifying thoughts), reinforcement of changes and providing strategies for dealing with weight regain [1].

3.2.2 Physical Activity

Encouragement should be given to increase levels of physical activity, regardless of whether this will lead to weight-loss. This is due to the general fitness improvements it can bring and the associated reduced risk of cardiovascular disease and type 2 diabetes. This may comprise of 45-60 minutes of moderate-intensity exercise per day, increasing to 60-90 minutes for those who have already lost weight to prevent regaining of excess weight. Suitable activities include brisk walking, gardening, cycling, supervised exercise programmes, swimming, stair-climbing etc [1].

3.2.3 Dietary

Dietary interventions should not be unduly restrictive but should be tailored to individual food preferences and also be nutritionally balanced. As with physical activity, dietary improvements should be encouraged for reasons other than weight loss alone due to the associated health benefits which a balanced diet can bring. The primary requirement for a dietary intervention however is to reduce energy intake to a point below energy expenditure by approximately 600 kcal/day or by reducing fat content. This should be partnered with expert support and intensive follow-up. Low (800-1600 kcal/day) and very low (800 kcal/day or less) calorie diets should be used with some degree of caution due to issues around nutritional completeness [1].

3.2.4 Pharmacological Interventions

Pharmacological interventions should only be considered after behavioural, physical and dietary interventions have been started and evaluated. This applies especially to those service-users who have not achieved their target weight loss or have plateaued. It may also be utilised to maintain weight-loss as opposed to continuing weight loss [1]. Orlistat is the only pharmacological treatment for obesity currently recommended by NICE. This medication is a lipase inhibitor which works through preventing approximately a third of consumed fat from being absorbed, However in addition to the well-documented side effects, there are potential issues related to the heightened risk of kidney problems [26].

4 Findings

We searched Medline, Embase, Cochrane Library, TRIP database and NICE Evidence on the 22nd June 2017 using the strategy detailed in the Search Strategy section. We included the 2014 Second Registry Report of the UK National Bariatric Surgery Registry as a key source for our review.

For the assessment of clinical effectiveness and safety, we identified a recent Cochrane systematic review of randomised controlled trials (RCTs) with a search date in November 2013 [23]. In addition to this, we therefore included only systematic reviews and meta-analyses with search dates after that of the Cochrane review, together with any more recently published randomised controlled trials (RCTs). However, for any comparisons not included in the Cochrane review, we included systematic reviews, meta-analyses, and RCTs published in the last ten years.

For the assessment of cost effectiveness, we identified a 2009 Health Technology Assessment (HTA) with a search date in August 2008 [27]. In addition to the HTA report, we therefore included only economic evaluation studies (cost effectiveness, cost-utility, cost-benefit, cost-consequence studies) published after that date.

We excluded studies of the following procedures no longer in current use (as per the approach taken by the 2014 Cochrane review):

- Jejunoileal bypass
- Horizontal gastroplasty
- Vertical banded gastroplasty or vertical gastroplasty (not banded)
- Banded gastroplasty that is not adjustable
- Banded gastric bypass
- Biliopancreatic diversion (without duodenal switch).

The search was also limited to English language publications and we excluded conference papers, letters, commentary and editorials.

4.1 Evidence of effectiveness

4.1.1 Clinical effectiveness

In addition to the Cochrane systematic review by Colquitt et al, we found three more recently published systematic reviews and five RCTs. Of the systematic reviews, the first, by Hachem et al, was published in 2015 [28]. and the second, by Cheng et al, was published in 2016 [29]. In addition to these, a third review investigating mortality, cardiovascular events and cancer outcomes was published by Zhou et al in 2016 [30].

The review by Hachem et al includes seven trials (n=2,281), one RCT and six non-randomised controlled trials (NRCT) and looks exclusively at quality of life (QoL) outcomes. Because of this it will only be discussed in the quality of life section of this rapid review.

The systematic review and meta-analysis, conducted in China by Cheng et al [29] pooled results from 25 RCTs, comparing surgical to non-surgical interventions in obese patients (BMI > 30 kg/m^2). The review included subgroup analyses, sensitivity analyses and assessment of publication bias. Of the 25 trials included, 12 covered the ‘severe obesity’ BMI range (BMI > 35 kg/m^2). Whilst this straddles the range being investigated in this rapid review, the majority of studies covered a BMI of more than 40 kg/m^2.

The review by Cheng et al was investigated but not included due to several concerns about the methodology used, particularly the meta-analyses. Chief amongst these is the considerable level of heterogeneity reported by the authors, an issue previously recognised by Colquitt et al and the reason for the lack of meta-analyses in the Cochrane review. The reasons for this heterogeneity are a combination of differences in surgical procedures, non-surgical interventions and chemical examination techniques. I^2 values (a statistical technique for quantifying heterogeneity) are predominantly above the 50% threshold of substantial heterogeneity as specified by the Cochrane Handbook for Systematic Reviews of Interventions [31]. Although sub-group analyses have been performed by Cheng et al in an effort to counteract heterogeneity, this means a reduction in the power of the analysis for individual sub-groups would be expected. In addition to this, it appears that sub-groups were established post-hoc rather than being pre-specified. This approach constitutes data-dredging according to the Cochrane Handbook for Systematic Reviews of Interventions, a technique which makes it possible to identify false explanations for heterogeneity [32].

Cheng et al's review included the same seven papers included by Colquitt et al which investigated differences between surgical and non-surgical weight-loss interventions. Two of the additional studies included by Cheng et al are included in this rapid review, however an additional eight trials were identified by Cheng et al that were not captured by Colquitt et al. On inspection, these were found to be not relevant to this rapid review for reasons relating to the study design (e.g. not being an RCT), the BMI range, the age of participants, use of surgical procedures that are not used in the UK or a focus on outcomes that are of low relevance.

Similar issues were present in the systematic review and meta-analysis performed by Zhou et al [30]. In this moderate quality study, the authors found substantial heterogeneity amongst the included trials and this is likely to be due to the aforementioned reasons of differences in participants, interventions, outcome definitions and study design. Of the comparisons made which did not show substantial heterogeneity amongst the included RCTs (as measured by I^2 values), statistically significant findings were not identified. The authors also encountered issues with the follow-up time and samples sizes of the included RCTs, ultimately concluding that the evidence from RCTs was inadequate for assessing the long-term effects of bariatric surgery for their selected outcomes. It should be noted that all RCTs included by Zhou which are relevant to this rapid review have been included as part of Colquitt et al's Cochrane review or are discussed as an individual RCT in the body of this rapid review.

For these reasons the findings reported by Cheng et al and Zhou et al have not been incorporated into this rapid review (other than in summary form in Evidence Table 1) and Colquitt et al remains the anchoring paper. It should be noted however that, despite our concerns with the methodology used, Cheng et al and Zhou et al's findings are consistent with those reported by Colquitt et al.

In this section of the report, we provide a brief overview of the methodology of the two systematic reviews before going on to describe their results alongside, where relevant, those from any individual RCTs identified. Detailed findings of the systematic reviews and individual studies are summarised in the evidence tables.

Systematic reviews

Colquitt 2014

The Colquitt study was a well-conducted systematic review published in 2014 which included seven RCTs [33, 34, 35, 36, 37, 38, 39] comparing surgical procedures to non-surgical therapy (n=618) and which followed a rigorous procedure. Five of the seven studies which were included (Dixon 2008 [33], Dixon 2012 [34], Liang 2013 [36], Mingrone 2012 [37] and O'Brien 2006 [38]) had adequate allocation sequence generation, with one of these (O'Brien 2006 [38]) having adequate concealment of allocation.

A small number of limitations were identified with the Cochrane review and are specified in Evidence Table 1. These include how representative the participants of the included studies are, with the majority being female, aged on average between 30 and 50 years, and morbidly obese. This may limit the generalisability of the findings, particularly considering the greater benefit which may be derived from younger adults who have a longer period to accrue benefits. Moreover, participants in the reviewed studies may not fully represent those seen in clinical practice, because many trials focused on low risk patients and, until recently in the UK, much surgery was performed on more unwell and more obese patients with more advanced complications. Lastly, we cannot determine whether study participants underwent tier 3 (or equivalent) non-surgical interventions before surgery.

The authors of the Cochrane review encountered difficulties combining results of these studies for meta-analysis so, instead, discussed the results narratively. The reason for this is the observed heterogeneity in the study characteristics, thought to be caused by variation in the characteristics of the participants, interventions and comparators. These reasons are consistent with those commented on by Cheng et al. The lack of a meta-analysis also precluded the possibility of performing planned sub-group analyses (e.g. whether clinical effectiveness varies by baseline BMI, so as to support a higher BMI threshold to that set by NICE).

Hachem 2015 [28]

This moderately well conducted systematic review by Hachem et al [28] included six studies (five non-randomised controlled trials and one RCT, n=2,281) comparing gastric bypass or gastric banding (both open and laparoscopic) with non-surgical management in obese adults (BMI >30 kg/m^2). In one of the included studies the mean BMI was below 40 kg/m^2 for all treatment arms and a further three studies had a single treatment arm which fell below this threshold. Presence of co-morbidities were not discussed in Hachem et al’s review and so these studies fall outside of the scope of this rapid review. Heterogeneity is not discussed in the review and it is unclear if a meta-analysis was intended by the researchers or not. Studies were included if they were English language, published in a peer-reviewed journal and examined QoL outcomes using standardised questionnaires. Most of the included studies reported non-surgical arms with a lower BMI than the surgical participants, potentially introducing some bias into the results. Follow-up times were variable, ranging from one month to ten years; few studies reported both short- and long-term QoL outcomes. The review is included as it provides a greater level of insight into quality of life improvements than the reviews by Colquitt et al or Cheng et al.

Randomised controlled trials

A further five individual RCTs were found comparing the clinical effectiveness and safety of bariatric surgery versus non-surgical interventions. These were published after the search date of the Cochrane review and were not included in the systematic review by Hachem. Two of these RCTs were included by Cheng et al but were deemed relevant to this review.

Halperin 2014 [40]

This single-centre, American RCT was based around the SLIMM-T2D trial and included participants with type 2 diabetes (n=38) who fell into one of two different BMI categories, below 35 kg/m^2 (n=13) or at least 35 kg/m^2 (n=25). Participants were randomised to receive either RYGB (n=19) or an intensive, multidisciplinary, medical diabetes and weight management programme called ‘Why WAIT’ (n=19). This non-surgical weight-loss intervention comprises a multidisciplinary approach which includes an endocrinologist, dietician, exercise physiologist, mental health provider and a diabetes nurse educator. It also includes regular medication adjustments, group exercise sessions, cognitive-behavioural therapy and group education. Selected participants were free from active cardiovascular or other diseases prohibiting them from engaging in exercise safely or undergoing a surgical procedure. Participants were also excluded if they had uncontrolled type 2 diabetes (defined as HbA1c levels above 12%), gastrointestinal disease, drug or alcohol misuse, weight loss greater than 3% within the past three months or were participating in other weight reduction programs. Metabolic assessments were performed at baseline and then repeated when 10% weight loss had occurred or at three months if this was not achieved. Final assessments were then performed at twelve months.

The study was limited by a lack of participants with diabetes-related complications, potentially limiting the generalisability of the findings. Despite randomisation, participants in the non-surgical arm had higher baseline HbA1c and fasting glucose levels, affecting the likelihood of achieving remission.

Ding 2015 [41]

This single-centre, American RCT was also based around the SLIMM-T2D trial and included participants with type 2 diabetes (n=40) who fell into one of two different BMI categories, below 35 kg/m^2 (n=15) or at least 35 kg/m^2 (n=25). Participants were randomised to receive either laparoscopic AGB (n=18) or the 'Why WAIT' programme (n=22). Assessments and follow-up were performed as described by Halperin et al, with baseline assessment being followed at 10% weight loss or three months and then at twelve months. This study followed an intention-to-treat methodology inclusive of all randomised participants who had been assessed at least once. The required sample size was calculated to be twenty-two participants per treatment arm in order to achieve 80% power, meaning the study may lack power to some extent. This was due to four surgery patients withdrawing consent and another being found to have severe aortic dilation. The included cohort was thought to be representative of a population with relatively advanced disease but had comparatively few patients with diabetes-related co-morbidities. It may therefore lack generalisability to a population with earlier, milder disease or those with more advanced diabetes-related complications.

Mingrone 2015 [42]

Mingrone et al conducted a single-centre RCT (n=60) in an Italian diabetes unit which allocated participants to receive either medical treatment (n=20), RYGB (n=20) or BPD (n=20). This study follows the same participants as the 2012 trial by Mingrone et al, included in the Cochrane review by Colquitt et al, allowing for a five year follow-up period [37]. Participants had a BMI of more than 35 kg/m^2 and a five year history of type 2 diabetes, exclusions were based on a history of type 1 diabetes, previous bariatric surgery, pregnancy, severe diabetes complications or other disorders and geographic inaccessibility.

Cummings 2016 [43]

Cummings et al undertook a single centre RCT comparing outcomes over 12 months of people aged 25-64 with type 2 diabetes and a BMI of 30 kg/m^2 to 45 kg/m^2. Participants were randomised to either laparoscopic Roux-en-Y gastric bypass (LRYGB) or intensive lifestyle and medical intervention (ILMI). Initially 23 people were randomised to the LRYGB intervention and 20 to the ILMI; however, 11 withdrew before an intervention so data for 15 participants in the LRYGB and 17 in the ILMI groups were gathered over the 12 months. The differences between those who participated and those who withdrew were significantly different in gender, disease severity and hypoglycaemic medication use. This RCT was underpowered with small numbers of participants.

Schauer 2017 [44]

Schauer et al conducted a parallel randomised controlled trial (the STAMPEDE study) in the US. This study follows the same participants as the Schauer 2012 [39] trial included in the Cochrane review by Colquitt et al. The study reports five year outcomes whereas the 2012 paper reported results after two years of follow up. Participants were randomised to receive either intensive medical therapy alone (n=50), intensive medical therapy with LRYGB (n=50) or intensive medical therapy plus laparoscopic sleeve gastrectomy (LSG, n=50). Following randomisation, eight patients in the medical therapy group and one patient in the LSG group withdrew whilst a further six were lost to follow up and one died after four years. Participants were between 20 to 60 years of age with a diagnosis of type 2 diabetes (glycated haemoglobin level >7.0%) and BMI of 27 kg/m^2 to 43 kg/m^2. Exclusions were based on previous bariatric or complex abdominal surgery, and poorly controlled psychiatric or medical conditions. There was potential bias in the results due to an imbalance of the proportion of people withdrawing from the medical intervention arm of the trial compared to the surgical interventions. The systematic review by Colquitt et al reported that five of the seven RCTs they included were considered to have adequate allocation concealment but Schauer (2012) (and therefore Schauer 2017) was not one of them.

Other studies

Subsequent to these initial findings, two further studies (summarised in evidence table 3) were identified through consultation with clinical experts.

Borisenko 2015 [45]

This study used a modelled population based on an adult, non-smoking, Swedish population aged 41 years with and without type 2 diabetes to investigate outcomes over a lifetime horizon. The study was stratified into BMI categories of 30-34 kg/m^2, 35-39 kg/m^2, 40-50 kg/m^2 and more than 50 kg/m^2. The study outcomes are unlikely to be generalisable to a UK population and the model also reported different proportions of bariatric procedures than are seen within the UK. Post-surgical weight regain is not accounted for in the model and no co-morbidities other than type 2 diabetes are modelled. There were several inconsistencies noted between the values quoted in the abstract and text of this paper compared to what was listed within various tables and supplementary documents. However, despite these drawbacks it was felt that the insight into lifetime risk of events was relevant to this rapid review.

Gulliford 2016 [46]

A recently released Health Services and Delivery Research report by Gulliford et al investigated the effects of bariatric surgery on individuals with a BMI of more than 35 kg/m^2 using a matched cohort design (n=3,045) and Markov analysis. This study was included due to its large size, its direct relevance to the UK population and reflection of UK clinical practice. The Clinical Practice Research Datalink (CPRD) was used as the source of electronic health records (EHRs) for this study. Data held within CPRD, which comprises anonymised longitudinal patients records from UK general practices, are considered to be broadly representative of the UK population. The aim of this study was to use the cohort study data to:

- evaluate weight changes in the absence of bariatric surgery
- report the costs of health-care utilisation associated with obesity
- analyse the realistic impact of bariatric surgery on diabetes incidence and remission, and on clinical depression
- model the realistic cost effectiveness of bariatric surgery over a lifetime from a UK perspective.

In particular, the study provides important insights into the impact of bariatric surgery on diabetes risk and remission, described in more detail below.

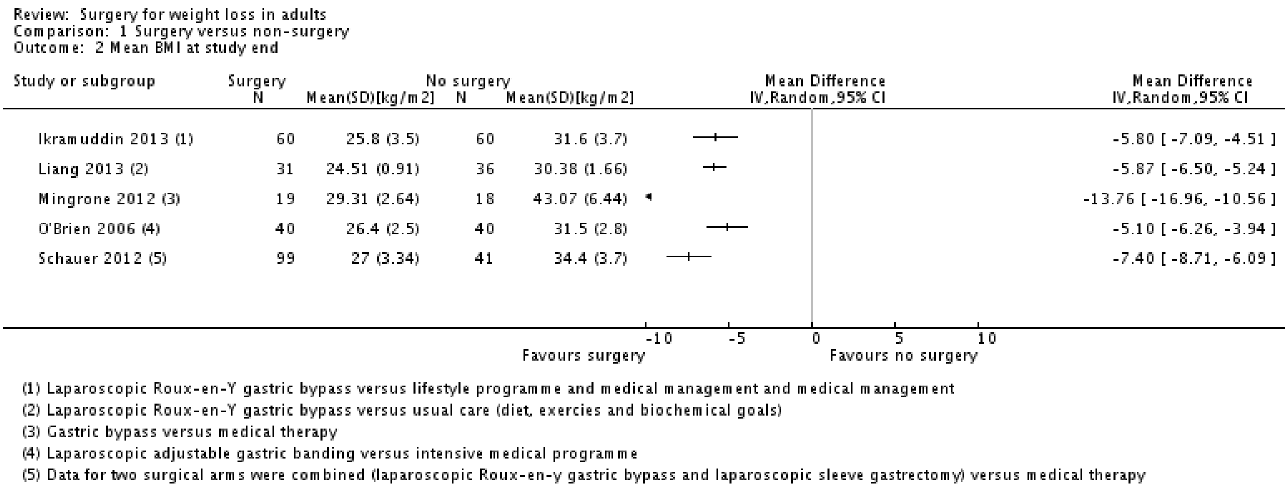
Bariatric surgery outcomes

The findings of the systematic reviews and individual studies are now described for different outcomes of bariatric surgery: weight loss, quality of life, and obesity-related co-morbidities.

Weight loss

In all seven RCTs reviewed by Colquitt et al, the mean BMI was lower following surgery than following non-surgical interventions [23] Five of these studies reported figures at a level of detail which could be analysed as a forest plot (see Figure 10). Of the seven RCTs included by Colquitt, four reported a mean BMI reduction which was greater than non-surgical therapy after either one year (Schauer 2012 [39]) or two years (Dixon 2008 [33], Dixon 2012 [34] and Mingrone 2012 [37]). In addition to this, surgical participants in four studies included by Colquitt et al (Ikramuddin 2013 [35], O'Brien 2006 [38], Schauer 2012 [39] and Dixon 2012 [34]) had significantly lower absolute weight at follow-up than non-surgical participants (p<0.001 or 95% confidence interval). The percentage of initial weight lost was reported by five studies included in the Colquitt review (Dixon 2008, Dixon 2012, Mingrone 2012 and O'Brien 2006) and this was routinely greater amongst surgical participants than non-surgical (p<0.001).

Figure 10: Forest plot showing surgical vs non-surgical BMI reduction for RCTs included in Colquitt systematic review [23]



Source: Colquitt et al. Surgery for weight loss in adults. Cochrane Database Syst Rev 2014 [23]

Updates for two of the trials included by Colquitt et al were published by Mingrone et al in 2015 [42] and Schauer et al in 2017 [44]. Mingrone et al is a single-centre, Italian RCT including participants (n=60) with a BMI of at least 35 kg/m^2 and type 2 diabetes. Surgical groups saw a reduction in BMI by 12.7 kg/m^2 (RYGB, n=20) and by 14.3 kg/m^2 (BPD, n=20) compared to a reduction by 3.3 kg/m^2 in the fifteen participants receiving medical treatment (p<0.0001) after five years.

Schauer et al 2017 [44] reported change in body weight, BMI, waist circumference and waist to hip ratio at five years follow up of an RCT comparing surgery (LRYGB n=49 and, LSG n=47) with medical therapy (n=38). All comparisons showed improvement for all measures after LSG and LRYGB compared to medical intervention (p<0.05). The reduction in body weight was greater after LRYGB than LSG (p<0.01).

Amongst the other individual studies identified, the RCT by Ding et al (2015)[41] investigated participants (n=45) with a BMI of between 30 kg/m^2 and 45 kg/m^2 and type 2 diabetes for at least one year. Although 37.5% of participants fell outside the BMI range of interest, the study reported a greater degree of weight loss after 12 months in participants who received a surgical (LAGB, n=23) intervention when compared to patients receiving intensive medical diabetes and weight management treatment (n=22) (13.5 kg vs 8.5 kg, p=0.027). The single-centre RCT by Halperin et al [40] compared LRYGB (n=19) against the 'Why WAIT' program (n=19). Findings were stratified by BMI classifications of less than 35 kg/m^2 (n=15) and at least 35 kg/m^2 (n=25), both with type 2 diabetes. Reductions in BMI were statistically significantly greater in the group randomised to surgery (p<0.001) after 12 months. Similarly, body-fat reduced by an average of 22.7 kg in the participants randomised to receive LRYGB, compared to 6.2 kg for those participating in the Why WAIT programme (p<0.001).

Cummings 2016 [43] reported changes in body weight, body fat and lean body mass between participants with diabetes receiving surgery and those receiving ILMI. All measures improved within each group over the 12 month period but they were greater in the surgical group than the ILMI group. Weight loss at one year was 25.8% ± 14.5% in the surgical group compared with 6.4% ± 5.8% (p<0.001) in the ILMI group. Body fat was lower within and between groups at baseline and one year (p<0.05). At 12 months follow up, lean body mass did not significantly decrease amongst participants in the ILMI arm of the trial but did in those who received surgery (p<0.05).

Quality of life

Colquitt identified two RCTs (Dixon 2012 [34] and O'Brien 2006 [38]) which compared validated measures of health-related quality of life between surgical and non-surgical interventions. One of these (O'Brien 2006 [38]) used the short form health survey (SF-36) [47] at a follow-up time-frame of two years between LAGB and a non-surgical group and identified statistically significantly higher scores for the surgical group in five out of eight domains. The second study (Dixon 2012 [34]) reported for the same time-frame and also utilised the SF-36 methodology. In this instance, Dixon (2012) identified statistically significantly greater improvements from baseline which were identified in two of the eight domains for surgical participants. Dixon (2012) also investigated the physical and mental SF-36 domains separately, reporting a statistically significant improvement in LAGB participants (p=0.04) for the physical component score but no statistically significant difference in the mental component summary score (p=0.92).

The systematic review by Hachem et al [28] of six studies (five NRCT and one RCT) reported greater improvements in quality of life in patients undergoing gastric bypass or gastric banding (both open and laparoscopic) than those undergoing non-surgical management. Of the included studies, two NRCTs reported statistically significant improvements when comparing surgical to non-surgical interventions, with the remaining studies commenting on pre- and post-operative differences between the groups. Four out of the six studies (one RCT and three NRCTs) using the SF-36 QoL measure saw improvements in physical QoL after bariatric surgery and three NRCTs out of six studies which used the SF-36 QoL measure saw improvements in mental QoL after bariatric surgery. This review included some studies where the mean BMI was less than 40 kg/m^2 but provides a greater level of insight into quality of life improvements and is included for that reason. Most of the included studies reported non-surgical arms with a lower baseline BMI than the surgical participants, perhaps introducing some bias into the results. Follow-up times were variable, ranging from one month to ten years. Few studies reported both short- and long-term QoL outcomes and most used a generic QoL measure, such as SF-36, which may not accurately capture weight-related changes. Various different questionnaires were used by the included trials, this combined with inconsistent reporting of results made drawing comparisons difficult. This was compounded by the fact that few studies made statistical comparisons between groups to identify significant differences. In addition to these points, Hachem et al faced similar issues to Colquitt et al relating to the heterogeneity of studies which covered differing surgical procedures and non-surgical interventions.

The RCT by Halperin et al reported that the Impact of Weight on Quality of Life Questionnaire (IWQOL) score improved significantly more in RYGB participants than in non-surgical participants (p<0.01). However, significant differences were not identified using other QoL frameworks [40, 48].

Whilst not reported in the initial 2012 study by Mingrone et al [37] (included in the Colquitt review [23]), the 2015 follow up paper [42] reports that improvements in QoL (measured using SF-36 methodology) were statistically significantly greater in surgically treated patients than in those receiving medical treatment after five years (p<0.0001).

Cummings et al [43] used the EQ5D questionnaire at baseline and 12 months follow up to assess change in quality of life. For both the LRGYB and ILMI groups overall health ratings improved (p=0.02, 0.035 respectively) and there were no between group differences (p=0.34).

Schauer (2017) [44] reported some quality of life measures at five years follow up which hadn't been available in Colquitt's review [23] of Schauer (2012) [39] reporting two year outcomes. The responses to a RAND 36-item health survey were collected at baseline and at five year follow up. In general health scores, patients receiving LRYGB and LSG but not medical therapy showed significant mean changes within group from baseline to five years (LRYGB p<0.001, LSG p<0.001, medical therapy p=0.92). There were no changes in bodily pain scores within group for the surgical interventions (LRYGB p=0.77, LSG p=0.87). In the medical therapy group none of the quality of life elements improved significantly from baseline; bodily pain (p=0.01) and emotional well-being (p=0.04) significantly worsened. Patients in both surgical groups had significant improvements in physical functioning (LRYGB p=0.002, LSG p=0.01) and energy/fatigue elements (LRYGB p=0.001, LSG p=0.001) but emotional wellbeing worsened significantly among patients receiving LRYGB (p=0.03). There were no differences between baseline and follow up after any intervention for social functioning, limitations due to emotional problems or limitations due to physical health.

Obesity-related co-morbidities

Of the seven RCTs comparing surgical to non-surgical interventions in Colquitt's systematic review, all reported the effects of interventions upon co-morbidities, however the reported co-morbidities varied across the studies. These are discussed in the following sections, with findings from additional studies incorporated where relevant.

Type 2 diabetes

Five of the RCTs included by Colquitt et al (Dixon 2008 [33], Ikramuddin 2013 [35], Liang 2013 [36], Mingrone 2012 [37] and Schauer 2012 [39]) reported outcomes related to type 2 diabetes for which the evidence was of moderate quality (see Table 4). One study (Dixon 2008) found that the remission rate of type 2 diabetes was statistically significantly higher after two years in participants receiving LAGB (73% vs 13% for conventional therapy, p<0.001). In addition to this, a larger proportion of LAGB participants no longer needed diabetes medication (83% vs 15% in conventional therapy), though this was not tested for statistical significance. Ikramuddin (2013) reported that HbA1c levels dropped to below 6% in 44% of participants receiving LRYGB after 12 months, whereas HbA1c levels fell to this level in 9% of those receiving a lifestyle programme with medical management (NICE recommends a target of 6.5% for adults with type 2 diabetes). In the same study, a greater proportion of participants experienced diabetes remission in the LRYGB group (90%) as opposed to none of those receiving usual care or usual care plus exenatide (a diabetes medication) therapy. Mingrone (2012) reported that after two years, 75% of participants receiving gastric bypass experienced diabetes remission compared to none amongst those receiving medical therapy (p<0.001), however, it is unclear if this study used an intention-to-treat methodology. Comparing LRYGB or LSG against intensive medical therapy, Schauer (2012) found that surgery yielded greater proportions of patients achieving a below threshold level of HbA1c (LRYGB 42%, LSG 37% and intensive medical therapy 12%). Schauer (2012) reported that more patients receiving surgery (LRYGB and LSG) stopped taking diabetes medication compared to those receiving medical therapy (78%, 51% and 0% respectively, p<0.05).

Table 4: RCTs of surgery versus non-surgery for diabetes, overview of results from Colquitt et al [23]

Study	Outcome	Surgery	No surgery	P value
Dixon 2008 [33]	Remission of type 2 diabetes at 2-years	22/30 (73%)	4/30 (13%)	RR 5.5 (95% CI 2.2 to 14.0); p < 0.001
	No diabetes medication at baseline	2/29 (6.9%)	4/26 (15.4%)	-
	No diabetes medication at baseline at 2 years	26/29 (89.7%)	8/26 (30.8%)	-
Ikramuddin 2013 [35]	% with fasting glucose <100 mg/dl at 12 months, n (%)	25 (44%)	7 (14%)	OR 5.8 (95% CI 2.1 to 15.9)
	% with HbA1c < 6.0% at 12 months, n (%)	25 (44%)	5 (9%)	OR 7.9 (95% CI 2.7 to 23.4)
	% with HbA1c < 7.0% at 12 months, n (%)	43 (75%)	18 (32%)	OR 6.0 (95% CI 2.6 to 13.9)
Liang 2013 [36]	Diabetes remission at 12 months: LRYGB v no surgery	28/31 (90%)	0/36 (0%)	-
	Diabetes remission at 12 months: LRYGB v no surgery + exenatide	28/31 (90%)	0/34 (0%)	-
Mingrone 2012 [37]	Diabetes remission at 2 years, n/N (%)	15/20 (75%)	0/18 (0%)	p < 0.001
Schauer 2012 [39]	Glycosylated haemoglobin ≤6% at 12 months, n (%): LRYGB	21 (42%)	5 (12%)	p = 0.002
	Glycosylated haemoglobin ≤6% at 12 months, n (%): LSG	18 (37%)	5 (12%)	p = 0.008
	n (%) of patients taking no diabetes medications: LRYGB	38 (78%)	0	p < 0.05
	n (%) of patients taking no diabetes medications: LSG	25 (51%)	0	p < 0.05

The follow up study by Mingrone et al in 2015 [42] noted that type 2 diabetes remission rates peaked at two years follow-up, with a degree of relapse seen at five years. RYGB saw a 75% remission rate at two years, falling to 37% at five years. No medical patients experienced remission and this difference between surgical and non-surgical arms was statistically significant (p<0.0001).

The update by Schauer (2017) [44] reported that, among the 134 patients who completed five years of follow up, two (5%) in the medical therapy group, 14 (28.6%) in the RYGB group and 11 (23.4%) in the LSG group achieved a glycated haemoglobin level of 6.0% or less. The differences between medical and surgical groups were statistically significant (for RYGB versus medical therapy p=0.003; for LSG versus medical therapy p= 0.02 in favour of surgery). There was no difference in the change of glycated haemoglobin between the two surgical groups (p=0.488). Duration of diabetes of less than eight years was the main predictor of achieving a glycated haemoglobin level of 6% or less (p=0.008).

The number of patients taking no diabetes medication at five years was 22 (45%) in the RYGB group and 11 (25%) in the LSG group (between surgical groups p<0.05 in favour of RYGB). All those who received medical therapy were taking medication at five years.

Halperin et al [40] found that RYGB led to a greater proportion of participants achieving a target HbA1c level than the non-surgical group (58% vs 16%, p=0.03) at 12 months. In addition to this the change from baseline was significantly greater after 12 months in participants receiving RYGB than the non-surgical group.

No significant differences in HbA1c or fasting plasma glucose levels were identified by Ding et al [41] however it should be noted that the population of this study consisted of participants with relatively advanced type 2 diabetes with comparatively few related complications.

Cummings et al [43] found that the primary endpoint of diabetes remission in their study (glycated haemoglobin ≤ 6% and no diabetes medications) at one year was achieved in 60% of participants in the RYGB group and 5.9% who received intense lifestyle and medical interventions (p=0.002). The odds ratio for diabetes remission at one year after RYGB compared with intense lifestyle and medical interventions was 19.8 (95% CI 2.0, 194.65, p=0.003).

Gulliford et al[46] identified that the incidence of diabetes per 1000 person-years was 5.7% (95%CI 4.2 – 7.8) in the surgical group, compared to 28.2% (95%CI 24.4 – 32.7) in the non-surgical cohort. This is an important finding which highlights that patients receiving surgery remain at risk of developing type 2 diabetes in the years following surgery; however this risk is much reduced when compared to those not receiving surgery. In addition to this, the rate of remission amongst surgical participants is substantially higher than amongst non-surgical participants, ranging from 30% to 17% in the five years following surgery. This compares to a range of 4% to 6% remission in non-surgical participants.

Cardiovascular risk and hypertension

Three RCTs reported by Colquitt et al (Dixon 2008 [33], Mingrone 2012 [37] and Ikramuddin 2013 [35]) investigated the differential effects of weight management interventions on hypertension (see Table 5). Two of these (Dixon 2008 and Mingrone 2012) reported greater reductions in the use of hypertension medication at two years amongst those receiving surgery and Mingrone (2012) also reported a greater proportion of surgical patients experiencing a reduction in systolic blood pressure below a threshold of 130mm Hg. Mingrone et al’s 2015 [42] follow-up paper was consistent with these findings, reporting that a greater proportion of medically treated participants (73%) required antihypertensive drugs than participants receiving RYGB (58%, P=0.0359).

Table 5: Surgery versus non-surgery for hypertension, overview of results from Colquitt et al[23]

Study	Outcome	Surgery	No surgery	P value
Dixon 2008 [33]	Antihypertensive agents at baseline, n/N (%)	20/29 (70%)	15/26 (57.7%)	
	Antihypertensive agents at 2 years, n/N (%)	6/29 (20.7%)	15/26 (57.7%)	
Ikramuddin 2013 [35]	% with systolic BP < 130 mm Hg at 12 months, n (%)	48 (84%)	44 (79%)	OR 1.7 (95% CI 0.6 to 4.6)
Mingrone 2012 [37]	Reduction/discontinuation of antihypertensive therapy, %	80%	70%	

In contrast to Colquitt and Mingrone's findings, Ding et al [41] identified a statistically significant greater reduction in systolic blood pressure from baseline at 12 months after non-surgical intervention than LAGB (P=0.038). Halperin et al [40] compared RYGB to the 'Why WAIT' programme and found that both systolic (P=0.02) and diastolic (P=0.001) blood pressure were lower at one year in participants receiving RYGB surgery.

Schauer 2017 [44] reported no significant changes in blood pressure between baseline and five years between or within the three intervention groups whereas Cummings et al reported a decrease in systolic blood pressure (but not diastolic) from baseline to 12 months in the surgical group (p=0.003) but not in the lifestyle and medical therapy group (p=0.23).

Metabolic syndrome

Colquitt et al reported on metabolic syndrome, however varying definitions of this were used by the included studies. Four RCTs included by Colquitt et al (Dixon 2008, Dixon 2012, O'Brien 2006 and Schauer 2012) identified reductions in proportions of participants with metabolic syndrome which were greater amongst those receiving a surgical intervention. Dixon (2012) reported the proportion of participants who had metabolic syndrome after two years compared to those with metabolic syndrome at baseline. This was lower (53%) in the laparoscopic adjustable gastric banding group than the conventional therapy group (92%), with the changes from baseline (-47% and -8% respectively) differing significantly between the groups (p=0.005) [34]. This was reinforced in findings by O'Brien (2006) who identified that the proportion of participants with metabolic syndrome after two years was 2.7% in the LAGB group and 24% in the intensive medical programme group despite both starting at a baseline value of 37.5% [38]. This difference was statistically significant (p<0.006). Schauer (2012) identified that a greater proportion of surgical participants experienced resolution of metabolic syndrome when compared to medical therapy alone [39].

Lipids

Lipid normalisation was reported by two studies included by Colquitt et al (Dixon 2008 and Mingrone 2012). Dixon (2008) reported reductions from baseline in the use of lipid-lowering agents after two years follow-up, these reductions being greater amongst those receiving LAGB as opposed to conventional therapy (27.6% vs 3.9%). Mingrone (2012) [37] reported on normalisation of lipids after two years, these being significantly greater in the GB group as opposed to the medical therapy group (100% vs 27.3%, P<0.001). The same direction of change was also identified for HDL cholesterol (100% vs 11.1%, P<0.005) and triglycerides (85.7% vs 0%, P<0.001). One study included by Colquitt (Ikramuddin 2013) et al found no difference in the proportions with LDL cholesterol below 100 mg/dL after one year between those receiving LRYGB with a lifestyle programme as opposed to a lifestyle programme alone [35].

At five years follow up Schauer (2017) [44] found the decrease from baseline in triglyceride levels (RYGB versus medical therapy p=0.03, LSG versus medical therapy p=0.04, RYGB versus LSG p=0.47) and increase in high density lipoproteins (RYGB versus medical therapy p=0.012, LSG versus medical therapy p=0.016, RYGB versus LSG p=0.75) were significantly greater in the two groups receiving a surgical intervention compared to the medical therapy group. Low density lipoproteins did not change either between or within the three intervention groups.

Ding et al reported that a greater proportion of LAGB patients achieved reductions of LDL cholesterol below threshold (p=0.019) than those participating in the 'Why WAIT' programme [41]. In addition to this, a greater reduction in use of lipid-lowering medication was observed in LAGB participants (p=0.029). Similar results were seen by Halperin et al when comparing RYGB against the 'Why WAIT' programme. In this trial, triglycerides were lower at one year in the surgical group (P=0.02) when compared to those receiving the non-surgical intervention (p<0.001), with HDL cholesterol increasing only in the surgical group.

Cummings et al [43] observed a decrease in triglycerides (LRYGB p=0.005 and ILMI p=0.002) and an increase in HDL cholesterol (LRYGB p=0.0004 and ILMI p=0.02) between baseline and 12 months in both the ILMI and surgical groups.

Obstructive sleep apnoea

Colquitt et al identified a single study (Dixon 2012) [34] looking at the effects of LAGB versus conventional weight-loss therapy on obstructive sleep apnoea (OSA). The proportion of participants who achieved mild OSA after two years was greater in the surgical group (27% vs 7%, p=0.04). However, one participant in the non-surgical group achieved remission of OSA, compared to none in the surgical group. Also, the proportions of participants who continued to use continuous positive airway pressure after two years did not differ significantly between the groups in this study. These findings are of some interest as Dixon's findings support the notion that bariatric surgery is more effective at driving weight loss over a two year period, with the surgical group achieving a mean weight loss of 27.8 kg compared to just 5.1 kg amongst the conventional therapy group (p<0.001). Both surgical and non-surgical groups reported a significant reduction in Apnoea-Hypopnea Index (AHI)[1] measurements with a decrease of 25.5 events/hour (reducing from 65.0 events/hour to 39.5 events/hour) in the surgical group and 14.0 events/hour (reducing from 57.2 events/hour to 43.2 events/hour) in the conventional group, however the between-group differences were not statistically significant. A post-hoc analysis showed a statistically significant positive relationship between change in weight and change in AHI (r = 0.45, p<0.001). However, when treatment arms were examined separately, the relationship was present only in the conventional therapy group. Dixon concluded that improvements in AHI tend to come from mild to moderate weight loss, with less benefit being realised as the degree of weight loss increases. This indicates a potentially complex picture around resolution of sleep apnoea from weight loss; additional factors such as age, sex and bony structures may contribute to this. The clinical picture may be further complicated by self-reported measures of quality of life, sleepiness and sleep quality. The large variance in the effects of weight loss on AHI may also indicate the study was under powered. In addition to this, the surgical procedure used (LAGB) is associated with a slower rate of weight loss than other techniques such as gastric bypass. The limited follow-up period of the study was such that a procedure which generates weight loss at a faster rate may have produced more measurable effects.

[1] The Apnoea–Hypopnea Index is an index used to indicate the severity of sleep apnoea. It is represented by the number of apnoea and hypopnea events per hour of sleep.

4.1.2 Safety

All seven studies included in the Colquitt systematic review reported information on complications and additional operative procedures; however, criteria for these differed between studies. No deaths were reported in any of the seven trials included in the review but all reported adverse events from surgery (such as operative interventions, revision surgery, port site infection) and from non-surgical interventions (such as medication intolerance, gastrointestinal problems and operative intervention requirement).

Dixon (2008) reported several adverse events amongst 30 surgical participants receiving LAGB. These included a superficial wound infection (one patient), gastric pouch enlargement requiring revision (two patients), eating difficulties and persistent regurgitation requiring band removal (one patient), post-operative febrile episode (one patient), minor hypoglycaemic episode (one patient), and gastrointestinal tract intolerance to metformin (one patient). Amongst the 30 non-surgical participants receiving conventional therapy minor adverse events associated with their medication were encountered, including gastrointestinal problems (two patients), persistent diarrhoea with metformin (one patient), and vasculitic rash (one patient). Other adverse events included multiple hypoglycaemic episodes (one patient), angina and a transient cerebral ischaemic episode requiring admission to hospital (one patient) and intolerance to very low-calorie meal replacement (two patients) [33].

Dixon (2012) reported 14 adverse events amongst participants receiving LAGB compared to 13 in the conventional therapy group. Serious event frequency was the same (17%) in each group, with both treatment arms reporting five events. Serious events in the surgically treated group were cholecystitis with pancreatitis, pouch dilation requiring repositioning, pneumonia, severe headaches and strangulated umbilical hernia. Serious adverse events in the conventional therapy group were acute abdomen, asthma, cardiac and renal failure, angina and peri-anal abscess and fistula. Minor adverse events were experienced by 40% of the participants in the LAGB group compared with 30% of participants in the conventional therapy group. Five participants in each group were hospitalised during follow-up [34].

Ikramuddin (2013) reported a total of 22 serious adverse events in the surgical group compared with 15 in the non-surgical group. Revision surgery was undertaken on one patient in the surgical intervention group but there were no conversions to other surgical interventions for weight loss [35].

Liang (2013) did not report complications or adverse events in detail but stated that there were no serious adverse events or deaths in any of the three treatment groups [36].

Mingrone (2012) reported no deaths and three surgical participants experiencing late complications compared to two medical participants experiencing persistent diarrhoea due to metformin use [37]. In their 2015 follow-up study, Mingrone et al [42] reported that after five years, there had been five major diabetes complications amongst four participants receiving medical therapy, including a fatal myocardial infarction. This compares with only one complication resulting from surgical intervention in the same time period. Mingrone (2015) also reported a higher incidence of metabolic adverse events amongst the surgical group than the medical treatment group after five years. Two surgical complications were noted, consisting of an intestinal occlusion in a RYGB recipient and an incisional hernia in a BPD patient, although the latter is of less relevance due to BPD not being in common usage in the UK.

A higher proportion of adverse events was noted by O'Brien (2006) [38] among non-surgical therapy participants (58%, n = 31) than in the laparoscopic adjustable gastric banding group (18%, n = 39). Non-surgical adverse events consisted of intolerance to orlistat (26%), acute cholecystitis (13%), the need for operative interventions (13%) and intolerance to very low calorie diet (3%). Surgical adverse events included operative interventions (13%), laparoscopic revision (prolapse or posterior) (10%), 5 mm port site infection (2.6%), and acute cholecystitis (2.6%).

Schauer (2012) [39] reported that proportionally more patients who underwent L RYGB (22%, n = 11) were hospitalised due to a serious adverse event than patients who underwent sleeve gastrectomy (8%, n = 4) or medical therapy alone (9%, n = 4). Proportionally more patients who underwent LSG (80%, n = 39) and medical therapy alone (81%, n = 35) had a hypoglycaemic episode during the 12 months following surgery than patients who underwent LRYGB (56%, n = 28) [39]. Schauer (2017) [44] updated adverse events reported from this cohort of patients through to five years follow up. Excessive weight gain (5% increase in body weight over baseline) was reported in eight (19%) patients in the medical therapy group but none in either of the groups receiving a surgical intervention. Anaemia was reported by significantly more patients ($p<0.05$) in the LSG group (n=24, 49%) compared to either the LRYGB (n=14, 28%) or medical therapy group (n=7, 16%). Mild anaemia (mean haemoglobin level 11.9 ± 1.5 g/dl) was more common in the two surgical groups than the medical therapy group ($p<0.009$). Hypoglycaemic episodes were reported in significantly fewer patients ($p<0.05$) receiving RYGB (n=32, 64%) than LSG (n=40, 82%) or medical therapy (n=39, 91%).There was one late reoperation converting LSG to LRYGB due to a recurrent gastric fistula.

Amongst the three additional RCTs identified by Ding et al [41] and Halperin et al [40], and Cummings et al [43] the former of these reported four serious adverse events amongst surgical participants (one failed band placement, two prolonged hospital stays and one surgical intervention for syringomyelia) and one non-surgical participant experienced ischaemic heart disease requiring coronary artery bypass surgery [41]. Halperin et al [40] reported that adverse events amongst surgical participants included ischaemic heart disease with coronary artery bypass surgery, a new breast cancer diagnosis, nephrolithiasis, exacerbated depression with suicide attempt and hip arthroplasty (though hip pain preceded enrolment and did not improve following weight loss). Amongst non-surgical participants, three pre-syncope serious adverse events were reported. During the year of follow up Cummings et al reported 64 adverse events in the ILMI group compared to 31 in the LRYGB group. These included 43 hypoglyceamic events in the lifestyle and medical therapy group, four of which were severe (blood glucose <2.2 nmol/l, or 3.3 nmol/l with neuroglycopenic symptoms) versus 16 in the LRYGB group none of which were severe.

As noted by Colquitt et al, deaths and adverse incidents tend to be rare events. The results reported in the papers included here are unlikely to provide a clear indication of the true prevalence of these events. This is further exacerbated by the limited size and duration of the studies identified for inclusion, as well as the variation seen amongst the recording thresholds used. Not all adverse events reported are necessarily causally related to the interventions that participants were enrolled to.

Bariatric surgery performed in the UK is considered to be a relatively safe procedure, particularly considering the high-risk patients often referred for these procedures [49]. Information from the UK Bariatric Surgery Registry confirms this, reporting 11 deaths over the three financial years 2011-2013, an overall post-operative mortality rate of 0.07% for this time period [22]. This compares favourably with studies performed in the USA with mortality rates reported of 0.1% to 0.3% [22]. A recent meta-analysis of 259 studies published worldwide reported an overall 30 day mortality rate of 0.08% in included RCTs and 0.22% for observational studies [22].

4.1.3 Cost effectiveness

Adults with BMI ≥ 40 kg/m^2, no co-morbidity (Evidence Table 4)

We initially found five published studies suitable for inclusion where the costs and/or cost effectiveness had been estimated for patients who had undergone bariatric surgery procedures. The studies either clearly stated that they included patients with a BMI of at least 40 kg/m^2 or BMI of at least 35 kg/m^2 with at least one co-morbidity, or if this was not explicit but the initial BMI was high, we assumed that some of the patients included had co-morbidity.

One of these was a systematic review by Wang and Furnback (2013) [50] of six economic evaluations for the cost effectiveness of bariatric surgery. Five of the included economic evaluations modelled the cost effectiveness over the lifetime; one study used a ten year timeframe. The focus of the review was to identify and discuss the different methodological approaches that have been used in economic evaluation of bariatric surgery. Meta-analysis of these six studies was not possible due to methodological differences as well as heterogeneity between the interventions, country of origin and time horizon. Despite these differences, they found that bariatric surgery in general is cost effective, particularly LRYGB and LAGB, which were both approximately US$5,000 to US$6,000 per QALY over a lifetime time horizon, well within usually accepted cost effectiveness thresholds. None of the studies included in the systematic review were based on UK costs.

These findings were consistent with an economic evaluation by Clegg et al (2003) [51] which was included in the review by Terranova et al (2012) [52]. Clegg et al reported that over a 20 year timeframe the ICER for LRYGB and LAGB was £6289 and £8527 per QALY respectively for patients for patients who meet the current NICE criteria for bariatric surgery. This estimate is however approximately 15 years out of date.

There were two economic evaluations based on longitudinal analysis of observed patients in the USA [53, 54].The first of these matched the study cohort (n=29,820) with patients with similar health profile but no bariatric surgery [53]. They found that bariatric surgery (including open and laparoscopic RYGB and LAGB) did not reduce over health care costs utilised by insured patients over the six post-operative years studied.

The second study by Finkelstein et al 2013 [54] also assessed costs against a matched sample using US health insurance data, including 31,184 observed patients, 9,104 of whom had a diagnosis of type 2 diabetes. They report that bariatric surgery costs are redeemed after approximately two years and that there is an average net cost saving of at least US$60,000 compared to non-surgical management of morbidly obese patients. in people with a BMI of more than 40 kg/m^2 and type 2 diabetes, the time to break even is reduced to less than two years and the potential cost savings are significantly greater (due to reduction in ongoing type 2 diabetes treatment costs).

It is not clear if the net cost savings can be extrapolated beyond five years and if this is at the same rate. We note that these costs are resource utilisation costs and that they do not take into account benefit (in terms of quality or life years) to the patient. Compared to the random matched sample, bariatric surgery was less cost effective. Given that morbid obesity was not an identified diagnosis in this group, it is perhaps inappropriate for them to be identified as a comparator.

Neither of these two USA studies report cost effectiveness of the different techniques in terms, costs and outcomes (quality of life and life years); rather, the focus is on health resource utilisation which may equate to costs to a health care commissioner.

We found one UK prospective economic evaluation of 88 patients in Scotland [55]. Cost effectiveness was not reported but the NHS perspective resource utilisation focus of the study showed that, at the median follow up of two years, bariatric surgery resulted in reduced co-morbidity (including type 2 diabetes, obstructive sleep apnoea and hypertension). The consequence of this improvement in co-morbidity was a net saving of £11,452 per annum for the related medications and nearly £20,000 per annum for hospital admissions and appointments.

Adults with BMI ≥ 35 kg/m^2 and type 2 diabetes mellitus (Evidence Table 5)

We found three studies reporting cost effectiveness for bariatric surgery for adults with a BMI of at least 35 kg/m^2 and a significant co-morbidity. All of these studies focused on patients with type 2 diabetes.

The updated HTA economic evaluation by Picot et al (2012) [56] compared LAGB only to usual diabetes care and reported the QALY gain, incremental costs and the incremental cost effectiveness ratio (ICER) at two to twenty years. The evaluation used outcomes data for the first two years, and then modelled outcomes and costs to 20 years. They found that at two years post-surgery, there was only 1% probability of LAGB being cost effective at £20,000/QALY (assuming that weight loss is gradual over the 2 year period), but that over a 20 year time horizon, LAGB is highly cost effective with an estimated ICER of £1,634/QALY.

The authors noted that the QALY gains identified for laparoscopic AGB are very modest (as usual diabetes care is also associated with QALY gains) and the cost effectiveness of the surgery is highly dependent on the high costs of diabetes care. If the excess weight loss was more modest, the estimated utility per BMI unit would be less. If surgical costs increased (including post-operative costs, ongoing band adjustments etc.) or if the cost of pharmacological diabetes care was reduced, then this would also reduce the cost effectiveness of laparoscopic AGB significantly.

More recently, Hoerger et al (2010) [57] published a Markov model simulation looking at patients aged 45 to 54 years with a BMI 35 kg/m^2 or more and type 2 diabetes. They estimated the cost effectiveness of LRYGB or LAGB in both patients with newly diagnosed (no more than five years after diagnosis) and established (at least ten years after diagnosis) type 2 diabetes, using six years of outcomes data from a large US registry study and then modelled over the lifetime of the patient. They found that both bariatric procedures are highly cost effective over the lifetime for patients with type 2 diabetes (newly diagnosed and established). However, the greatest cost effectiveness was reported for patients with newly diagnosed type 2 diabetes who underwent laparoscopic RYGB. The sensitivity analysis suggests that the cost effectiveness is improved further in patients aged 35 to 44 years.

It also suggests that the cost effectiveness is reduced (by a factor of two) if the initial BMI is only 30 to 35 kg/m^2. Consistent with the UK HTA economic evaluation by Picot et al (2012), Hoerger et al also found that the cost effectiveness of bariatric surgery was highly dependent on the cost of usual diabetes care [56, 57].

A 2006 study by Ackroyd et al (2006) was referenced in a review of cost effectiveness by Terranova et al (2012) [52, 58]. This reported the UK cost per QALY of both LAGB and LRYGB to be under £2000 per QALY over the first five years after operation.

Adults with BMI ≥ 40 kg/m^2 and BMI ≥ 35 kg/m^2 with co-morbidity (mixed population) (Evidence Table 6)

We initially found five published studies suitable for inclusion where the costs and/or cost effectiveness had been estimated for patients who had undergone bariatric surgery procedures. The studies either clearly stated that they included patients with a BMI of at least 40kg/m^2 or BMI of at least 35 kg/m^2 with one or more co-morbidities, or if this was not explicit but the initial BMI was high, we assumed that some of the patients included had co-morbidity.

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The second study by Finkelstein et al 2013 [54] also assessed costs against a matched sample using US health insurance data, including 31,184 observed patients, 9,104 of whom had a diagnosis of type 2 diabetes. They report that bariatric surgery costs are redeemed after approximately two years and that there is an average net cost saving of at least US$60,000 compared to non-surgical management of morbidly obese patients. in people with a BMI of more than 40 kg/m^2 and type 2 diabetes, the time to break even is reduced to less than two years and the potential cost savings are significantly greater (due to reduction in ongoing type 2 diabetes treatment costs).

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Subsequent to these initial findings, two further studies were identified through consultation with clinical experts. Since these two studies include both clinical effectiveness and cost effectiveness findings, they are covered in both sections of this report.

One of the studies (Borisenko et al 2015) was a cost effectiveness model based upon registry data from Sweden, where the case mix did not reflect UK current clinical practice. The model attempted to estimate (based upon two year post-operative outcomes data from the Swedish Obesity Surgery registry) the costs and benefits associated with bariatric surgery compared to optimal medical management (OMM) over a lifetime, as well as the impact of a three year delay to receiving surgery. This included stratifying patients groups (by gender, initial BMI and diagnosis of diabetes) to estimate differential cost effectiveness.

The model estimated that surgery was more likely to result in a lower lifetime absolute risk of diabetes in particular (14% vs 36% OMM, no p-values reported) and that, for the whole cohort, bariatric surgery was highly cost effective (estimated lifetime ICER €2050 per QALY). In addition, bariatric surgery was cost saving at 17 years post-surgery. More detailed subgroup modelling reported that over a lifetime, surgery was cost saving in all patients except for non-diabetic adults with a BMI lower than 35 kg/m^2.

The authors found that the overall lifetime cost of treatment would be increased if patients with diabetes or a BMI greater than 40 kg/m^2 waited for more than three years to receive bariatric surgery. This was due to loss of clinical benefit which resulted in a reduction of 0.6 life years and 1.2 QALYs per patient over a lifetime.

Recurrence of T2DM had been included in the model design, however we noticed some inaccuracies in the published report (including review of the data supplement for further detail about the results) which gave rise to concern about the reliability of the estimated cost effectiveness estimates. In addition we noted (as did the authors) that the case mix was not reflective of UK current clinical practice and that perhaps the reason that the lifetime estimate ICER was so low might be due to:

- Omission of weight regain post bariatric surgery
- Omission of recurrent diabetes post-surgery
- No annual costs of post-surgery support (e.g. ongoing nutritional and psychological support).

Despite these methodological weaknesses and likely overestimate of cost savings and cost effectiveness (in terms of the ICER), this study is consistent with previous studies in finding that bariatric surgery is a highly cost effective intervention with a low cost per QALY.

Most recently, a UK NIHR funded study was published 2016. This was a combination of a matched cohort study (using data from the UK Clinical Practice Research Datalink (CPRD) which comprises anonymised longitudinal patients records from UK general practices and is considered to be highly representative of the UK population overall) and a cost effectiveness model. This study found that, over a lifetime, bariatric surgery resulted in both additional QALYs and was highly cost effective with an ICER of £7129 (95%CI £6775 to £7506) per QALY. The ICER for patients with severe obesity alone was slightly higher at £7675 per QALY, but still well within UK accepted norms. The authors found that bariatric surgery was particularly cost effective in patients with morbid obesity and T2DM (£6176 per QALY).

Unlike the findings of Borisenko et al the authors of the NIHR report [46] did not find bariatric surgery to be cost saving over the lifetime but this may be because the model included a wider range of costs associated with the bariatric surgery care pathway as well as a more realistic estimate of diabetes remission and recidivism.

This study is perhaps the most reliable and authoritative estimate of the lifetime ICER. It is higher than the estimate from some of the other studies but it was based upon UK matched cohort data and UK Bariatric Surgery Registry data and included multivariate sensitivity analyses.

4.2 Evidence Summary Tables

Evidence Table 1: Summary of systematic reviews of bariatric surgery vs non-surgical interventions

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
1a	Colquitt 2014 [23] *(Cochrane Review)* Systematic review of RCTs	"Adults who are overweight or obese as defined by the study" Whilst most studies included BMI ≥ 35 kg/m^2 with co-morbidities and BMI ≥ 40 kg/m^2, some studies also included subjects with BMI < 35 kg/m^2. (n=618, 7 RCTs)	Bariatric Surgery (AGB, RYGB, RYGB plus medical therapy, SG plus medical therapy, RYGB plus lifestyle programme) (n=316)	Non-Surgical Interventions (Conventional therapy, Intensive Medical Programme, Medical Therapy, Lifestyle programme with medical management, Usual care) (n=302) Comparison 1 (2 RCTs): Lap AGB vs Conventional Therapy Group (BMI 30-40 with T2DM, BMI 35-55) Comparison 2 (1 RCT): Lap AGB vs Intensive Medical Programme (BMI 30-35 with co-morbidity) Comparison 3 (1 RCT): Gastric Bypass vs Medical Therapy (BMI ≥35 kg/m^2 with T2DM) Comparison 4 (1 RCT): Lap RYGB/Lap SG plus medical therapy vs medical therapy alone (BMI 27-43	**Apparently meaningful difference (no p-values or 95% CIs reported)** *Note that because results could not be pooled in a meta-analysis they are reported here as apparently meaningful differences even if individual trials identified significant differences* • **Weight Loss** Compared with non-surgical interventions, surgery had a consistent effect on each of the outcome measures related to weight, regardless of the type of procedure • **Quality of Life** Two moderate quality studies reported greater improvements in SF-36 at 2 years for surgical patients than for non-surgical therapy • **Diabetes Remission** Five of the RCTs reported diabetes-related outcomes (patients with diabetes remission, diabetes medication or specified levels of glycosylated haemoglobin) Remission of type 2 diabetes after two years was statistically significantly ($p < 0.001$) higher following laparoscopic adjustable gastric banding (73%) than conventional therapy (13%) (RR 5.5; 95% CI 2.2 to 14.00) At 12 months, 44% of those in the laparoscopic Roux-en-Y gastric bypass group had a glycosylated haemoglobin level of < 6% compared with 9% in the lifestyle programme with medical management group A greater proportion of people with diabetes remission in a laparoscopic Roux-en-Y gastric bypass group (90%) than the usual care group (0%) or usual care and exenatide therapy group (0%)	• Publication bias not assessed due to low numbers of studies • Meta-analysis not performed due to differences in characteristics of participants, interventions and comparators. • Some studies were thought to not be free of selective reporting • No studies were based in the UK • Follow-up periods of 12, 18 and 24 months

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
				kg/m^2 with T2DM) Comparison 5 (1 RCT): LRYGB plus lifestyle programme vs lifestyle programme with medical management (BMI 30-39.9 kg/m^2 with T2DM) Comparison 6 (1 RCT): LRYGB with usual care vs Usual care with pharmacological treatment (BMI >28 kg/m^2 with T2DM)	After two years, 75% of those in the gastric bypass group but none of those in the medical therapy group were classed as having a diabetes remission ($p < 0.001$) Proportionally more participants in the laparoscopic Roux-en-Y gastric bypass plus intensive medical therapy and laparoscopic sleeve gastrectomy plus intensive medical therapy groups achieved a glycosylated haemoglobin level of ≤ 6% at 12 months than patients in the intensive medical therapy alone group (42%, 37% and 12%, respectively; $p = 0.002$ for gastric bypass versus medical therapy alone; $p = 0.008$ for sleeve gastrectomy versus medical therapy alone) A higher proportion of patients in gastric bypass and sleeve gastrectomy groups were taking no diabetes medications than in the medical therapy alone group (78%, 51% and none, respectively; $p < 0.05$ for gastric bypass versus medical therapy alone and for sleeve gastrectomy versus medical therapy alone) • **Hypertension** Improvements from baseline to two years follow-up for those in the laparoscopic adjustable gastric banding group compared to the conventional therapy group in their use of anti-hypertensives (49.3%versus 0%) The proportions of participants with a reduction/discontinuation of antihypertensive therapies were 80% in the laparoscopic adjustable gastric banding group and 70% in the conventional therapy group Another trial found no difference in the proportion of people with systolic blood pressure < 130 mmgHg (odds ratio (OR) 1.7, 95% CI 0.6 to 4.6) • **Lipids** Improvements from baseline to two years follow-up for those in the laparoscopic adjustable gastric banding group compared to the conventional therapy group in their use of lipid-lowering agents	

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
					(27.6% versus 3.9%) The proportion of participants with normalisation of lipids after two years was significantly higher in the gastric bypass group than the medical therapy group, for total cholesterol (100%versus 27.3%; p < 0.001), high density lipoprotein (HDL) cholesterol (100% versus 11.1%; p < 0.005) and triglycerides (85.7%versus 0%; p < 0.001) • **Sleep** The proportion of participants that achieved a diagnosis of 'mild' obstructive sleep apnoea after two years was statistically significantly higher in those treated with laparoscopic adjustable gastric banding (27%) compared with conventional therapy (7%) (p = 0.04) • **Adverse Events** No deaths reported overall several adverse events among people in the laparoscopic adjustable gastric banding group Frequency of serious adverse events was the same (17%) in both LAGB and conventional weight-loss groups Four early serious adverse events in the laparoscopic Roux-en-Y gastric bypass group but no events in the lifestyle programme group No serious adverse events or deaths in any of the LRYGB, no surgery and no-surgery + exenatide groups No operative deaths from gastric bypass, low numbers of late complications. Two participants in the medical therapy group had persistent diarrhoea associated with metformin A higher proportion of adverse events among those people in the non-surgical therapy group (58%, n = 31) than in the laparoscopic adjustable gastric banding group (18%, n =39)	

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
					Comparing LRYGB and LSG (each in addition to intensive medical therapy) with intensive medical therapy alone proportionally more patients who underwent gastric bypass (22%, n = 11) were hospitalised due to a serious adverse event than patients who underwent sleeve gastrectomy (8%, n = 4) or medical therapy alone (9%, n = 4)	
1a-	Hachem 2015 [28]	BMI>30 kg/m^2 7 trials compare surgical to non-surgical interventions (n= 2,281)	Gastric Bypass, Gastric Banding (open and Laparoscopic) (n=746)	Lifestyle intervention, medical treatment, non-seeking surgery (n=1,535)	**Apparently meaningful difference (no p-values or 95% CIs reported)** • Improvements in QoL outcomes were greatest in those undergoing bariatric surgery • 4 out of 6 studies using the SF-36 QoL measure saw improvements in physical QoL after bariatric surgery • 3 out of 6 studies using the SF-36 QoL measure saw improvements in mental QoL after bariatric surgery • One study found a significant change in both the surgical and non-surgical groups from baseline on the WRSM (weight specific QoL measure) on symptom distress and number of symptoms QoL at 1 year	• Systematically reviews 6 nRCT and 1 RCT • Meta-analysis not performed • Heterogeneity not discussed • Not all studies included are BMI >40 kg/m^2 • Most studies' non-surgical arms have lower BMI • Variable follow-up time from 1 month to 10 years • Few studies reported both short- and long-term QoL outcomes • 5 studies did not compare surgical to non-surgical groups but instead compared pre and post-operative data.
1a- (inconclusive)	Cheng 2016 [29]	BMI > 30 kg/m^2 16 trials,	SG, RYGB, LAGB, BPD	Non-Surgical Interventions (Conventional therapy, Intensive	**Apparently meaningful difference (no p-values or 95% CIs reported)** ***Note that due to heterogeneity issues, only results from meta-analyses with an I^2 value ≤50% are reported and sub-group analyses are excluded. Although P values are reported by Cheng et al, they should***	• Meta-analysis performed but I^2 figures reported indicate large degree of heterogeneity between

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
		(n=1,194)	(n=600)	Medical Programme, Medical Therapy, Lifestyle programme with medical management, Usual care) (n=594)	***be interpreted with caution due to methodological concerns*** • Waist circumference (cm) reduced by 14.59 cm (I^2=50%, p<0.00001) • Systolic pressure (mmHg) reduced by 3.5mmHg (I^2=11%, p<0.00001)	studies • Papers selected relevant to this review are also reported by Colquitt et al • Post-hoc sub-group analyses may lead to reduction in power • Different inclusion criteria to Colquitt et al with additional papers which are not relevant to this review included • Publication bias noted in the results • Findings consistent with Colquitt et al
1a- (inconclusive)	Zhou 2016 [30]	BMI > 30 kg/m^2 11 RCTs, (n=890)	RYGB, LAGB, DJBL, BPD-DS, SG, Implantable Gastric Stimulation (n=491)	Non-Surgical Interventions (Lifestyle intervention, medical intervention, gastric stimulation turned off) (n=399)	**All odds ratios reported for pooled RCT effects had confidence intervals which spanned one and so were not classed as significant.**	• Subgroup analyses to identify source of heterogeneity not possible because many studies included a mixed population • All the meta-analyses used the random-effects model • Separate analyses for RCT and non-RCT study designs • No significant publication bias detected for all-cause mortality, other outcomes not assessed due to insufficient data

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
						• Evidence from RCTs is limited because of the relatively short follow-up and small sample sizes • Not all surgical interventions are relevant to UK clinical practice

**see Appendix1*

Evidence Table 2: Summary of individual RCTs of bariatric surgery vs non-surgical interventions

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
1b	Schauer 2017 [44] Single centre RCT (the STAMPEDE study), USA	BMI 27-43 kg/m2 with T2DM Age 20-60yrs n=134	RYGB (n=49) LSG (n=47)	Medical therapy (n=38)	**Glycated haemoglobin ≤6%** predicted at 5 years if duration of diabetes <8 years at baseline (p<0.007). **Achieving 6% glycated haemoglobin** • Medical therapy group n=2 (5%) • LRYGB n=14 (28.6%) • LSG n=11 (23.4%) LRYGB vs medical therapy p=0.003 in favour of surgery LSG vs medical therapy p= 0.02 in favour of surgery. LRYGB vs LSG p=0.488 **% change in bodyweight** LRYGB vs medical therapy p<0.001 LSG vs medical therapy p<0.001 LRYGB vs LSG p=0.12 **% change in waist cm** RYGB vs medical therapy p<0.001 LSG vs medical therapy p<0.001 RYGB vs LSG p=0.122 **% change waist hip ratio** LRYGB vs medical therapy p<0.001 LSG vs medical therapy p=0.019 LRYGB vs LSG p=0.769 **Number of people taking no diabetes medications at Baseline and 5 years** LRYGB baseline n=0 (0%), 5 years n=22 (45%) LSG baseline n=1(2.1%), 5 years n=11(25%) Medical therapy baseline n=1(2.6%), 5 years n=1(2.5%) LRYGB vs LSG p<0.05 in favour RYGB **Fasting plasma glucose** LRYGB vs medical therapy p<0.003 LSG vs medical therapy p =0.02 LRYGB vs LSG p=0.35 **Decrease in triglyceride levels in favour of surgical groups** LRYGB vs medical therapy p=0.03 LSG vs Medical therapy p=0.04 LRYGB vs LSG p=0.47	• 5 year follow up of Schauer 2012 (2 year follow up reported in Colquitt et al) • BMI overlaps with range of interest but no stratification of results between <35 kg/m^2 and ≥35 kg/m^2 groups. • Large number of comparisons reported. Imputed intention to treat only carried out on primary end point (change in proportion of people with glycated haemoglobin ≤6%)

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
					Increase in HDL choleseterol in favour of surgical groups LRYGB versus medical therapy p=0.012, LSG versus medical therapy p=0.016, LRYGB versus LSG p=0.75. **QoL – within group differences baseline to 5 yrs** **General health scores** LRYGB p<0.001 (sig improved) LSG p<0.001(sig improved) Medical therapy p=0.92 (no change) **Bodily pain** LRYGB p=0.77 (no change) LSG p=0.87 (no change) Medical therapy p=0.01 (sig. worse) **Emotional wellbeing** LRYGB p=0.03 (sig worse) LSG p=0.62 (no change) Medical therapy p=0.04 (sig worse) **Physical functioning** LRYGB p=0.002 (sig improved) LSG p=0.01 (sig improved) Medical therapy p=0.39 (no change) **Energy/fatigue** LRYGB p=0.001 (sig improved) LSG p=0.001 (sig improved) Medical therapy p=0.32 (no change) **No significant statistical difference** Decrease in LDL within groups Decrease in blood pressure within groups Social functioning Limitations due to emotional or physical problems. **Adverse events** **Excessive weight** LRYGB n= 0 (0%) LSG n=0 (0%) Medical therapy 8 (19%) **Anaemia** LRYGB n=14, 28% LSG group n=24, 49% Medical therapy group n=7, 16%	

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
					LRYGB vs LSG p<0.05 (favouring RYGB) LSG vs medical therapy (favouring medical therapy) **Mild anaemia** Surgery vs medical therapy p<0.009 (favouring medical therapy) **Hypoglycaemic episodes** LRYGB n=32, 64% LSG n=40, 82% Medical therapy n=39, 91% Surgery vs medical therapy p<0.05 One conversion LSG to RYGB due to a recurrent gastric fistula.	
1b	Cummings 2016 [43] Single centre RCT USA	Age 25-64 yrs with T2DM BMI 30-45 kg/m2 n=32	RYGB (n=15)	Intensive lifestyle and medical intervention (n=17)	**Statistically significant difference** The odds ratio for diabetes remission at 1 year after LRYGB compared with intense lifestyle and medical interventions was 19.8 (95% CI 2.0, 194.65, p=0.003). • LRYGB cohort had longer diabetes duration than ILMI (p=0.009) • Weight loss greater in RYGB group (p<0.001) • Diabetes remission at 1 year was 60% with RYGB vs 5.9% ILMI (p=0.002) • Reduction in lean body mass was greater in RYGB group than ILMI (p<0.05) • Reduction in body fat was greater in RYGB group than ILMI (p<0.05) **Decrease in triglycerides within groups** LRYGB p=0.005 ILMI p=0.002 **Increase in HDL cholesterol within groups** LRYGB p=0.0004 ILMI p=0.02 **QoL** LRGYB and ILMI showed improvement in overall health ratings (p=0.02, p= 0.035 respectively) with differences between groups (p=0.34).	• BMI overlaps with range of interest in this review but no stratification of results between <35 kg/m^2 and ≥35 kg/m^2 groups. • Short follow up –(1 year) • Small sample size may limit power to detect changes.

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
1b	Ding 2015 [41] Single centre RCT, USA	BMI 30-45 kg/m^2 with T2DM for ≥1yr n=40	LAGB (n=18)	Intensive medical diabetes and weight management programme ('why WAIT' program) (IMDWM) (n=22)	**Statistically Significant Difference** • **Weight loss** LAGB group saw additional weight loss at 12 months (p=0.027) 13.5kg vs 8.5kg in non-surgical group • **Blood Pressure** Systolic blood pressure reduced more from baseline after non-surgical intervention than LAGB (p=0.038) • **Cholesterol** Greater proportion of LAGB patients achieved reductions of LDL cholesterol below threshold (p=0.019) Reduction in use of lipid-lowering medication in LAGB (p=0.029) **Apparently meaningful difference (no p-values or 95% CIs reported** • **Adverse Events** 4 adverse events reported in the LAGB group vs 1 in the IMDWM group **No statistically significant difference** • **Glycaemic control** Proportions achieving target HbA1c and fasting glucose levels were not significantly different • **Waist circumference** • **Use of hypertensives** • **Fitness**	• BMI range overlaps the range of interest (37.5% of participants outside the range of interest) • Gives a clear outline of the non-surgical intervention • Cohort had relatively advanced T2DM but few related complications • Follow-up is fairly short-term, longer term outcomes not evaluated • Results may not generalise to those with milder T2DM or with advanced complications • Only one type of surgical procedure evaluated

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
					(6 minute walk, post exercise heart rate) • **UKPDS risk scores** • **Quality of Life** SF-36, PAID, EQ-5D & Barriers to Being Active measures	
1b	Mingrone 2015 [42] Single centre RCT, Italy	BMI ≥35 kg/m^2 with T2DM n=60	RYGB (n=20), BPD (n=20)	Medical treatment (n=20)	**Statistically Significant Difference** • **T2DM remission** RYGB saw 75% remission at 2 years, reducing to 37% at 5 years due to relapse. BPD saw 95% remission at 2 years, dropping to 63% at 5 years. Zero medical patients saw remission (p<0.0001). • **Weight loss** Surgical groups saw a reduction in BMI of -12.7 (LRYGB) and -14.3 (BPD) compared to -3.3 in the medical treatment group (p<0.0001). • **Quality of Life** Surgical patients scored significantly better than medically treated patients for all sub-domains (p<0.0001) **Apparently meaningful difference (no p-values or 95% CIs reported)** • **T2DM Improvement** 31 out of 38 (82%) participants who relapsed after surgery were able to maintain HbA1c < 7% with little to no use of glucose lowering medication. • **Weight regain** Modest weight regain was observed in surgical groups between years 2 and 5, weight loss was stable in medical group • **Complications** Complications were observed for 4 medical participants and 1 surgical participant.	• BPD no longer performed in the UK • 2 medical participants excluded due to crossing over to surgery because of inadequate glycaemic control. • 5 year follow up period

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
					No statistically significant difference • Blood pressure	
1b	Halperin 2014 [40] Single centre RCT, USA	BMI <35 kg/m^2 and ≥35 kg/m^2, both with T2DM n=38	RYGB (n=19)	'Why WAIT' program (n=19)	**Statistically Significant Difference** • **Resolution of hyperglycaemia** 58% of theL RYGB group reached target HbA1c levels compared to 16% in the medical therapy group (p=0.03) • **Blood Pressure & Lipid Levels** Systolic (p=0.02) and diastolic (p=0.001) blood pressure and triglycerides (p=0.02) were lower at 1 year and high-density lipoprotein cholesterol was increased only in the LRYGB group (p<0.001) • **Cardiometabolic risk** Risk scores for coronary heart disease (p<0.001), fatal coronary heart disease (p<0.001), stroke (p=0.008), and fatal stroke (P=0.009) were all reduced more at 1 year after LRYGB than non-surgical intervention • **Weight Loss** Reduction in BMI at 12 months (p<0.001), waist circumference (p<0.001), fat mass (p<0.001) and lean mass (p<0.04) were all significantly greater in participants receiving surgery • **Patient reported outcomes** IWQOL score improved significantly greater in RYGB participants compared to non-surgical participants (p<0.01). **No statistically significant difference** • Fitness improvement	• Gives a clear outline of the non-surgical intervention • Includes patients with a BMI <35 kg/m^2 which is out of scope of this review • No stratification within the results between <35 kg/m^2 and ≥35 kg/m^2 groups • SLIMM-T2D trial • Wide range of diabetes duration and insulin use duration • Limited applicability to patients with extensive diabetes-related complications • Relatively short 12 month follow-up period • Small sample size may limit power to detect changes. • Adverse events discussed but absolute numbers not given for comparison

**see Appendix1*

Evidence Table 3: Summary of Additional Papers of Interest Regarding Clinical Effectiveness

<table>
<tr><th>Level of Evidence*</th><th>Study</th><th>Population</th><th>Intervention</th><th>Comparator</th><th>Outcomes</th><th>Comments</th></tr>
<tr>
<td>1b</td>
<td>Gulliford 2016 [46]

UK

Matched cohort study using analysis of UK CPRD[2] and Markov model</td>
<td>n=3,045

Adults with BMI>35kg/m^2

2002-2014</td>
<td>Bariatric surgery</td>
<td>n=247,537

(n=278,982 for analysis of probability of attaining normal body weight)

General population control

2008-2014</td>
<td>Primary outcomes:
• Weight changes in the absence of bariatric surgery
• Bariatric surgery and Incidence of type 2 diabetes mellitus
• Bariatric surgery in the management of type 2 diabetes mellitus
• Bariatric surgery and clinical depression

In the absence of bariatric surgery
Annual probability of achieving normal body weight
• Male, obesity: 1 in 210
• Female, obesity: 1 in 124
• Male, morbid obesity: 1 in 1290
• Female, morbid obesity: 1 in 677
Annual probability of achieving 5% weight reduction
• Male, morbid obesity: 1 in 8
• Female, morbid obesity: 1 in 7
Weight regain to value above initial weight in participants who lost 5% body weight:
• At 2 years: 52.7% (95%CI 52.4% to 53.0%)
• At 5 years: 78% (95%CI77.7% to 78.3%)

Diabetes incidence per 1000 person-years (bariatric surgery vs control): 5.7%(95%CI 4.2 to 7.8) vs 28.2%(95%CI 24.4 to 32.7)

Diabetes remission* (n=826) (maximum 5 year follow-up)
<table>
<tr><th rowspan="2">Cohort</th><th colspan="5">Years Follow-Up</th></tr>
<tr><th>1</th><th>2</th><th>3</th><th>4</th><th>5</th></tr>
<tr><td>Surgery</td><td>30%</td><td>25%</td><td>21%</td><td>21%</td><td>17%</td></tr>
<tr><td>No Surgery</td><td>4%</td><td>4%</td><td>3%</td><td>5%</td><td>6%</td></tr>
</table>
Reported as relative rate of remission within report

Depression:
Proportion of people with depression before and after bariatric surgery:
• Pre-surgery: 36%
• Post-surgery year 2: 32%
• Post-surgery year 7: 37%</td>
<td>UK, NHS perspective

Reflects UK clinical practice and costs

Lifetime horizon

Extensive sensitivity analyses included</td>
</tr>
</table>

[2] The UK Clinical Practice Research datalink (CPRD) is the world largest primary care database comprising anonymised longitudinal patient records from UK general practices. Electronic health record data are considered to be broadly representative of the UK population.

	Borisenko 2015 [45] Sweden Modelled outcomes over lifetime based on 2 year outcomes from Swedish Obesity Surgery Registry	Modelled population Based on 41 year old non-smoking adults with BMI 30-34, 35-39, 40-50 and >50 kg/m^2 With or without T2DM	Bariatric surgery Gastric bypass (98%) Sleeve gastrectomy (1.6%) Gastric band (0.4%)	Optimal Medical Management (OMM)	Lifetime absolute risk (surgery vs OMM) (no p-values reported) of events: • Diabetes: 14% vs 36% • Nonfatal MI: 22% vs 28% • Fatal MI; 2% vs 3% • Nonfatal stroke: 18% vs 23% • Fatal stroke: 3% vs 4% • TIA: 2% vs 2% • Heart Failure: 15% vs 19% • Pulmonary arterial disease: 10% vs11% Impact of 3 year delay to surgery: Delays in surgery may lead to a loss of clinical benefits: up to 0.6 life years and 1.2 QALYs per patient over a lifetime in those with diabetes or a body mass index >40 kg/m^2.	Recurrence of T2DM has been included in the model Outcomes not generalisable as • % different procedures are different to current UK practice. • Weight regain post bariatric surgery has not been factored in • Other obesity related co-morbidities not modelled

**see Appendix1*

Evidence Table 4: Cost effectiveness of bariatric procedures in adults with BMI ≥ 40kg/m^2 and no co-morbidity

<table>
<tr><th>Level of Evidence*</th><th>Study</th><th>Population</th><th>Intervention</th><th>Comparator</th><th>Outcomes</th><th>Comments</th></tr>
<tr>
<td>1b</td>
<td>Picot 2009 [56]

UK HTA systematic review and economic evaluation</td>
<td>Adults with BMI ≥40kg/m^2</td>
<td>LRYGB

LAGB</td>
<td>Non-surgical management</td>
<td>Over 20yr time horizon:
<table>
<tr><th></th><th>QALY gain</th><th>ICER</th></tr>
<tr><td>LRYGB</td><td>1.52 to 1.98</td><td>£3160 to £4127</td></tr>
<tr><td>LAGB</td><td>0.92 to 1.88</td><td>£1897 to £3863</td></tr>
</table>
</td>
<td>Modelled over 20yr time horizon

- Costs and outcomes both discounted at 3.5%

- Multi-way sensitivity analysis

ICER is highly dependent on procedure costs (including operating time and LOS). Varying costs and utilities still produced an ICER <£5,000 per QALY.

Assumed from references that gastric bypass and gastric band procedures were laparoscopic</td>
</tr>
</table>

<table>
<tr>
<td>4</td>
<td>Hernandez 2010 [59]

USA

Markov model</td>
<td>Adults with BMI ≥40 kg/m^2</td>
<td>Lap-RYGB

Lap-AGB</td>
<td>No surgery</td>
<td>
<table>
<tr><td>Age (yrs)</td><td>QALYs gained
(lap-RYGB over lap-AGB)</td></tr>
<tr><td>35-44</td><td>+7.8</td></tr>
<tr><td>45-54</td><td>+6.4</td></tr>
<tr><td>55+</td><td>+4.7</td></tr>
<tr><td>BMI(kg/m^2)</td><td>QALYs gained
(lap-RYGB over lap-AGB)</td></tr>
<tr><td>40</td><td>+2.8</td></tr>
<tr><td>50</td><td>+6.4</td></tr>
<tr><td>60</td><td>+9.6</td></tr>
</table>
</td>
<td>Modelled to 85yrs of age

Assumed no impact on QoL 2yrs (lap-RYGB) and 4yrs (lap-AGB) post-surgery

Focus was on morbidity directly caused by surgical techniques that led to re-operation.

Did not take into account co-morbidity.</td>
</tr>
</table>

see Appendix1

Evidence Table 5: Cost effectiveness of bariatric procedures in adults with BMI ≥ 35kg/m^2 and type 2 diabetes mellitus (T2DM)

<table>
<tr><th>Level of Evidence*</th><th>Study</th><th>Population</th><th>Intervention</th><th>Comparator</th><th>Outcomes</th><th>Comments</th></tr>
<tr>
<td>1b</td>
<td>Picot 2012 [56]

(update of Picot et al 2009) [27]

UK HTA systematic review and economic evaluation</td>
<td>T2DM

and

BMI>30 and <40kg/m^2</td>
<td>LAGB</td>
<td>Usual diabetes care</td>
<td>Cost effectiveness:
<table>
<tr><th></th><th>Incremental QALY gain over usual care</th><th>Incremental costs</th><th>ICER</th></tr>
<tr><td>@2yrs</td><td>0.27</td><td>£5359</td><td>£20,159</td></tr>
<tr><td>@5yrs</td><td>0.61</td><td>£3034</td><td>£4,969</td></tr>
<tr><td>@20yrs</td><td>1.10</td><td>£1792</td><td>£1,634</td></tr>
</table>

Sensitivity analysis:
<table>
<tr><th></th><th>WTP threshold</th><th></th></tr>
<tr><td></td><td>£20k/QALY</td><td>£30k/QALY</td></tr>
<tr><td>@2yrs</td><td>1%</td><td>38%</td></tr>
<tr><td>@20yrs</td><td>100%</td><td>100%</td></tr>
</table>

Non-surgical care is also associated with QALY gains at 2, 5 and 20 yrs respectively:

1.62, 3.74, 11.12 for usual diabetes care compared to 1.70, 4.03 and 11.52 for LAGB.</td>
<td>Population includes class I obesity (BMI>30<35kg/m^2) which out of scope of this review

- one way sensitivity analysis undertaken

- Costs and outcomes discounted at 3.5%

5 and 20yr data modelled (assumed that at 10 yrs, BMI, BP, lipid profile and T2DM relapses)

Cost effectiveness highly dependent on the (high) costs associated with T2DM case (83% total costs are T2DM costs)

QALY gains are modest.

Only LAGB is used – no LRYGB/LSG.</td>
</tr>
</table>

3b	Hoerger 2010 [57] USA Markov model	Adults aged 45-54years BMI≥35kg/m^2 and T2DM - newly diagnosed (nor more than 5 years after diagnosis) - established (at least 10 years after diagnosis)	Bariatric surgery comprising LRYGB LAGB	Usual diabetes care	Newly diagnosed T2DM: LRYGB: $7000/QALY LAGB: $11000/QALY Age 35-44 vs 65-74 years LRYGB: $5k/QALY vs $12k/QALY LAGB: $9-17k/QALY Established T2DM: LRYGB: $12000/QALY LAGB: $13000/QALY Age 45-54 vs 65-74 years LRYGB: $9k/QALY vs $18k/QALY LAGB: $11-18k/QALY Subgroup analyses BMI 30-34 kg/m2 reduces the cost effectiveness by a factor of two (lower BMI loss and lower QoL gain)	Assume (from references) that procedures are laparoscopic Based on 2005 US costs (US$) Model assumptions clearly stated Sensitivity analysis: model highly sensitive to the QoL improvement per BMI unit estimate and cost of treating active diabetes All scenarios were cost effective Younger patients are most cost effective.

4	Ackroyd 2006 [58] in Terranova 2012 [52]	BMI ≥35kg/m^2, with T2DM	Bariatric surgery including LAGB RYGB	Conventional medical therapy or non-surgical management	Over 5 year timeframe (direct costs only) LAGB: £1,929/QALY LRYGB: £1,517/QALY	Based on narrative outcomes from 1 (Ackroyd et al 2006) of 6 studies in review

**see Appendix1*

Evidence Table 6: Cost effectiveness of bariatric procedures in adults with BMI ≥ 40kg/m^2 or BMI ≥ 35kg/m^2 with co-morbidity (mixed population)

Level of Evidence*	Study	Population	Intervention	Comparator	Outcomes	Comments
1b	Gulliford 2016 [46] UK Matched cohort study using analysis of UK CPRD[3] followed by cost effectiveness analysis and Markov model	n=3,045 Adults with BMI>35kg/m^2 With or without co-morbidity 2002-2014	Bariatric surgery	n=247,537 (n=278,982 for analysis of probability of attaining normal body weight) General population control 2008-2014	Lifetime cost effectiveness of bariatric surgery compared to no surgery: • ICER: £7,129 (95%CI £6775 to £7506) per QALY • Incremental cost of bariatric surgery: £15,258 (95%CI 15,184 to 15,330; p<0.001) • Incremental QALY: 2.142(95% CI 2.031 to 2.256) For patents with morbid obesity and T2DM: • ICER: £6176 (95% CI £5894 to £6457) per QALY For patients with severe obesity: • ICER: £7675 (95%CI £7339 to £8037)	NHS perspective Reflects UK clinical practice and costs Lifetime horizon Extensive sensitivity analyses included Comparison is 'no surgery' which may include but is not restricted to NHS funded tier 2 and tier 3 interventions

[3] The UK Clinical Practice Research datalink (CPRD) is the world largest primary care database comprising anonymised longitudinal patient records from UK general practices. Electronic health record data are considered to be broadly representative of the UK population.

<table>
<tr>
<td></td>
<td>Borisenko 2015 [45]

Sweden

Modelled outcomes over lifetime based on 2 year outcomes from Swedish Obesity Surgery Registry</td>
<td>Modelled population

Based on 41 year old non-smoking adults with BMI 30-34, 35-39, 40-50 and >50 kg/m^2

With or without T2DM</td>
<td>Bariatric surgery

Gastric bypass (98%)

Sleeve gastrectomy (1.6%)

Gastric band (0.4%)</td>
<td>Optimal Medical Management (OMM)</td>
<td>Lifetime cost effectiveness of bariatric surgery compared to OMM (for all patients):

-€8408
+0.8 LYG
+4.1 QALYs
(€2050 per QALY)

For all patients (mixed population), surgery is cost saving at 17years.

Surgery is cost saving vs OMM over lifetime for all subgroups except for non-diabetic adults with a BMI <35 kg/m^2:

Surgery is highly cost effective for all sub-groups (less than £20,000 per QALY)
<table>
<tr><td></td><td colspan="5">ICER, €/QALY</td></tr>
<tr><td></td><td>Moderately obese (BMI 33kg/m^2)</td><td>Severely obese (BMI 37kg/m^2)</td><td>Morbidly obese (BMI 42kg/m^2), best-case</td><td>Morbidly obese (BMI 42kg/m^2), worst-case</td><td>Super obese (BMI 52kg/m^2)</td></tr>
<tr><td>male diabetic patients</td><td>-4406</td><td>-4189</td><td>-3340</td><td>-3343</td><td>-2854</td></tr>
<tr><td>female diabetic patients</td><td>-6740</td><td>-6310</td><td>-4668</td><td>-4803</td><td>-3990</td></tr>
<tr><td>male non-diabetic patients</td><td>449</td><td>-130</td><td>-1026</td><td>-970</td><td>-1484</td></tr>
<tr><td>female non-diabetic patients</td><td>51</td><td>-668</td><td>-1531</td><td>-1509</td><td>-2142</td></tr>
</table>

Impact of 3 year delay to surgery:
Overall lifetime cost of treatment may be increased in patients with diabetes or a body mass index >40 kg/m^2.</td>
<td>Recurrence of T2DM has been included in the model

Concern re accuracy as reported ICER at 2yrs is inconsistent with data in supplement (S5). Also ICER for Moderate obese male is 459 in text but 449 in supplement.

Outcomes not generalisable as

% different procedures are different to current UK practice.
Weight regain post bariatric surgery has not been factored in
No annual cost of post bariatric surgery support included over lifetime period
Other obesity related co-morbidities not modelled
</td>
</tr>
</table>

2c	Weiner 2013 [53] USA Longitudinal analysis of 2002-8 claims	n=29,820 insured patients BMI≥40 or BMI≥35 with co-morbidity hypertension 54.7%, T2DM 24.6% Others 7.4% Post-op observation period 1yr n=29,820 2yr, n=19,564 3yr, n=12,760 4yr, n=7,571 5yr, n=4,584 6yr, n=1,939	n=29,820 Bariatric Surgery including: ORYGB LRYGB LAGB	n=29,820 Matched non-surgical cohort	Total health care cost per year (including inpatient, outpatient and pharmacy costs), mean(SD),US$ (2005), surgery vs non-surgery 1yr pre-op: 8850(12542) vs 9590(21913) yr 1: 8905(18814) vs 9908(22192) yr 2: 9908(19273) vs 9264(21057) yr3: 9211(19263) vs 9041(21243) yr4: 9051(19520) vs9232(19819) yr5: 9386(21137) vs 8966(20270) yr6: 9259(26909) vs8714(27280)	USA costs may not be directly generalisable to UK. Large study: observed costs not modelled. Old data – outcomes may be better than observed in the study. ORYGB (34.5%)is an obsolete comparison now but is included in the surgical cohort. Provider costs not cost effectiveness. Costs also reflect pharmacy inflation Bariatric surgery does not reduce overall health care costs in the long term.

2c	Finkelstein 2013 [54] USA Non randomised case control study of MarketScan data (including 100 insurers)	Adults with BMI≥40, including some T2DM.	LRYGB n=21,533, 30.9% T2DM LAGB n=9,651, 25.4% with T2DM	Morbid obesity (MO), no surgery Matched random sample (same co-morbidity profile but no confirmed diagnosis of morbid obesity)	<u>Compared to diagnosed morbid obesity, no surgery</u> Time to break even (yrs) LABG: 1.5 (CI: 1.45 to 1.55) LRYGB: 2.25 (CI: 2.07 to 2.43) Net cost savings at 5 yrs (US$) LAGB: 78,980 (CI: 100,550 to 62,320) LRYGB: 61,420 (CI: 82,870 to 44,710) <u>For diabetes subset</u> Time to break even (yrs) LAGB: 1.25 (CI: 1.02 to 1.48) LRYGB : 1.75 (CI: 1.49 to 2.01) Net cost savings at 5 yrs (US$) LAGB: 127,590 (CI: 167,590 to 94,840) LRYGB: 103,340 (CI: 146,760 to 65,550)	Time to break even and cost savings are dependent on the comparator – untreated MO population or patients with same co-morbidity profile but no diagnosis of MO. Based on health care resource utilisation only. Does not reflect societal benefits or costs. Does not reflect the benefit (QoL/ADL) to patients. ? post 5 yrs Based on very large case control study outcomes.

2c	Karim 2013 [55] Prospective economic evaluative Single centre, Scotland 2008-11	Adults median age 45 years (25-65 yrs) Median BMI 47.3 (35-64.5) kg/m^2 n=88, some with Co-morbidities T2DM (n=29) Hypertension (n=31) Arthritis (n=20) Ischaemic heart disease (n=3) Obstructive sleep apnoea (n=27)	Bariatric surgery comprising LRYGB (n=19) LAGB (n=36) LSG (n=33)	Pre-surgery median	At median f/up 24 months (12-45 months): • BMI 35.79kg/m^2 (decreased 24% ($p<0.05$) Co-morbidities resolved/improved • T2DM: 22/29 (75.9%) • Hypertension: 15/31 (48.4) • OSA: 22/27 (81.5%) Medication net savings: £11,452 p.a. (39.5%) Hospital admissions/ outpatient clinics net savings: £18,950 p.a.	UK study Used average costs of resource utilisation from 2005 to April 2012. No breakdown of cost savings per procedure. No control group.

4	Wang and Furnback 2013 [50] Review of cost effectiveness studies (Faria 2013, Song 2013, WangWong 2013, Chang 2011, Maklin 2011, Campbell 2010)	BMI≥35kg/m^2 with co-morbidity Or BMI≥40kg/m^2	Bariatric Surgery including ORYGB LRYGB LAGB LSG	Ordinary treatment (ranging from brief intervention to intensive conservative treatment).	Bariatric surgery is cost effective, despite variation in methodology for forecasting cost effectiveness. Bariatric surgery produced additional life years compared to no surgery (from 78 years to 80-81 years) Cost effectiveness over lifetime (US$ per QALY) compared to no surgery ranged from: • Bariatric surgery(LAGB/LRYGB/LSG): 1,771-13,249 • LRYGB: 5,600 to 6,600 • LAGB: 5,400 to 6,200 • ORYGB: 17,300	Focus on studies that relate directly to bariatric surgery. Excluded papers that focused on long-term resolution of diabetes or other co-morbidities. No meta-analysis possible so outcomes from 6 studies are narrative only.
4	Clegg 2003 [51] in Terranova 2012 [52]	BMI >40 kg/m^2 and ≥35 kg/m^2 with co-morbidity	Bariatric surgery including LAGB RYGB VBG	Conventional medical therapy or non-surgical management	Over 20 year time frame, direct costs only RYGB: £6,289/QALY LAGB: £8,527/QALY VBG: £10,237/QALY	Based on only 1out of 6 studies in the review Costs are 16 years out of date (1999/2000)

*see Appendix1

5 Discussion and conclusions

5.1.1 Clinical effectiveness of bariatric surgery compared with non-surgical management in adults with obesity (BMI at least 35 kg/m^2)

Bariatric surgery was found to consistently achieve greater weight loss than non-surgical interventions.

All studies included by Colquitt et al [23] found statistically significant differences in weight loss for follow-up periods of one to two years, regardless of the surgical procedure or type of participants included. The quality of the evidence was moderate, with a noted lack of high quality RCTs comparing the long-term effects of surgery to conventional treatment amongst large sample sizes. Colquitt et al's findings were reinforced in RCTs performed by Ding et al [41], Halperin et al [40] and Cummings et al [43] as well as in the follow-up studies by Mingrone et al (2015) [42] and Scahuer et al (2017) [44]. Observed weight loss is also associated with a reduction in co-morbidities such as type 2 diabetes, metabolic syndrome and sleep apnoea but the benefits relating to hypertension and lipid profiles is less clear. With the exception of Gulliford et al's [46] seven year follow up of T2DM cases, there is a lack of longer-term data examining the effects on co-morbidities of surgery compared to non-surgical interventions. The findings pertaining to sleep apnoea provide a complex picture in terms of clinical benefit. Whilst surgery appears to lead to more patients achieving a classification of mild OSA, the benefits in terms of overall AHI improvements and requirement for CPAP do not differ significantly between patients undergoing surgery and those not undergoing surgery despite greater weight loss amongst surgical participants. This means that caution must be applied when communicating the possible benefits of bariatric surgery to patients and that patients must be evaluated carefully prior to making any recommendations around ceasing treatment for obstructive sleep apnoea after surgical intervention.

The available evidence is highly variable in terms of the interventions being investigated.

One fundamental issue with the evidence in this field is the wide variation in the type of non-surgical intervention used as a comparator and the generally poor descriptions of these given in the literature compared to the more precise descriptions of surgical procedures. Colquitt et al reported that a meta-analysis was considered to be inappropriate due to the inherent differences between studies in terms of participants, surgical interventions and non-surgical comparators.

More detailed descriptions of robust lifestyle interventions were provided by Ding et al [41], Halperin et al [40] and Mingrone et al [42], who each described interventions which bore a resemblance to tier 3 services as described by the Royal College of Surgeons. However, even in these instances where a well described lifestyle intervention was applied, surgical interventions still resulted in greater weight-loss, regardless of co-morbidities.

Those who do manage to achieve weight loss without surgery are likely to regain weight in the future.

Realistic outcomes for non-surgical weight loss in adults in the UK general population is reported by Gulliford et al highlighting the difficulty in achieving normal body weight or even just a 5% reduction in initial body weight without surgery. The authors also reported weight regain to a value greater than the initial weight in the participants who initially achieved 5% weight loss without bariatric surgery (52.7% of those who lost 5% of initial body weight at two years, rising to 78% at 5 years). This shows that, even amongst people who achieve a modest weight reduction without surgery, only a small proportion of them manage to avoid weight regain two to five years later.

Considering the weight of the observed evidence in favour of surgical interventions for weight loss and resolution of co-morbidities (particularly type 2 diabetes), it would seem reasonable to conclude that the provision of lifestyle interventions is a less clinically effective approach to dealing with more severe levels of obesity. The risks and benefits of surgery need to be carefully considered given the poor quality of information available in the literature pertaining to patient safety, however the data provided by the Bariatric Surgery Register goes some way toward countering these concerns.

5.1.2 Safety of bariatric surgery compared with non-surgical interventions

A direct comparison of patient safety between bariatric surgery and non-surgical interventions is not possible based on the available evidence.

Adverse incidents appear to be more common in surgical patients but it is difficult to draw firm conclusions due to inconsistent recording, different reporting methods and small numbers of incidences reported in the literature. The sample size of each study is generally small and no statistical comparisons have been made, merely narrative discussions. Whilst safety information related to bariatric surgery is readily available from the UK National Bariatric Surgery Registry, this information does not allow for comparison to the numbers and rates of non-surgical adverse events [22]. The lack of longer term studies precludes the possibility of identifying whether the higher weight loss amongst surgery patients may lead to a measurable and significant reduction in adverse events over longer periods than those observed, compared to a non-surgical cohort with a lesser degree of weight loss and increased time spent living with co-morbidities such as type 2 diabetes and hypertension.

5.1.3 Cost effectiveness of bariatric surgery compared to non-surgical management in adults with obesity (BMI at least 35 kg/m^2)

All of the economic evaluations are weak due to the limited long-term follow-up data available to inform post-trial modelling.

In addition, there was significant heterogeneity between the studies including different:

- Populations (age, initial BMI, number of co-morbidities);
- Bariatric surgery techniques;
- Comparators (surgery or different levels of non-surgical intervention);
- Cost outcomes;
- Duration of model (two year to lifetime estimates);
- Assumptions about the trajectory of weight change (both time period and weight loss);
- Perspective - immediate hospital costs only versus lifetime costs and patient quality of life and life years);
- Evaluation methodology and sensitivity analyses (none, one way or multivariate);
- Country and setting (which affects the generalisability of the findings to UK NHS setting).

There is no single answer to the question of cost effectiveness of bariatric surgery compared to non-surgical management.

For patients with a BMI of more than 40 kg/m^2 and no co-morbidity, there is reliable evidence from the UK HTA evaluation over a 20 year time horizon that bariatric surgery is highly cost effective with the ICER estimated to be less than £5000 per QALY for both LRYGB and LAGB.

For patients with a BMI of more than 35 kg/m^2 and type 2 diabetes, the ICER is estimated to be circa £20,000 per QALY over two years. When this observed data is modelled over the 20 year time horizon, the ICER is £1634 per QALY, indicating that bariatric surgery (LAGB) is highly cost effective.

Over a lifetime, bariatric surgery results in both additional QALYs and is highly cost effective.

For a mixed population, the most reliable and authoritative estimate of the lifetime ICER was from the recently published cohort study and cost effectiveness analysis by Gulliford et al (2016) [46]. It is higher than the estimates from some of the other studies such as those by Wang and Furnback [50] and Borisinko et al [45]. but it was based upon UK matched cohort data from the UK CPRD and UK Bariatric Surgery Registry data and included multivariate sensitivity analyses.

This study found that over a lifetime, bariatric surgery resulted in both additional QALYs and was highly cost effective with an ICER of £7129 (95%CI £6775 to £7506) per QALY. The ICER for patients with severe obesity alone was slightly higher but, at £7675 per QALY it was still well within UK accepted norms. The authors found that bariatric surgery was particularly cost effective in patients with morbid obesity and T2DM (£6176 per QALY).

Unlike the findings of Borisenko et al, the authors of the NIHR report did not find bariatric surgery to be cost saving over the lifetime but this may be because the model included a wider range of costs associated with bariatric surgery as well as a more realistic estimate of diabetes remission and recidivism.

Significantly, all the studies that we included clearly indicated that bariatric surgery (particularly if performed laparoscopically which is current UK clinical practice) is highly cost effective when using the NICE ‘usual’ cost effectiveness threshold of £20,000 to £30,000 per QALY, and even against the more recently calculated ‘affordable’ NHS threshold estimated by Karl Claxton et al of circa £12,000 per QALY [60]. Whilst we have limited data to be able to reliably estimate the actual cost per QALY for bariatric surgery overall or for each bariatric technique, the reported ICERs are consistently lower than the £20,000 per QALY ceiling by a factor of between four and ten (depending on the estimate considered). NHS commissioners can be confident that bariatric surgery (based on the studies identified in this review) is highly cost effective.

In terms of which bariatric surgery procedure is the most cost effective, there is insufficient reliable evidence to clearly identify a single procedure or to reliably differentiate between the cost effectiveness of LRYGB and LAGB (frequently reported in the studies). Reports by Finkelstein et al (2013) [54] are comparably cost effective, with similar estimated cost per QALY over a lifetime (LRYGB: US$6,600 vs LAGB: US$6200), similar time to break even (LRYGB: 2.25 years vs LAGB: 1.5 years for patients without co-morbidity) and similar net cost savings over five years (LRYGB: US$103,340 vs LAGB: US$127,590).

Laparoscopic RYGB appears to offer greater QALY gain which offsets the additional cost of the procedure. Laparoscopic AGB is similarly cost effective, largely because the procedure costs are so much lower.

5.1.4 Sub-groups who might benefit more from bariatric surgery than others (defined by, for example, initial BMI status and/or presence of a specific co-morbidity)

Individuals with type 2 diabetes who received surgery experienced higher rates of remission than those receiving non-surgical interventions.

Colquitt et al reported that all RCTs included in their review that examined type 2 diabetes as an outcome reported significantly higher remission rates amongst those receiving surgery compared to those using conventional therapy or dietary changes. This conclusion is backed by many of the additional studies included in this review. This is of particular interest due to the increasing direct and indirect costs of type 2 diabetes in the UK, which are estimated by Hex et al [61] to rise to £36 billion by 2036. Mingrone et al noted that although surgery was more effective than medical treatment in achieving long term control of type 2 diabetes in obese patients, continued monitoring of glycaemic control should be investigated due to the potential for relapse amongst some patients. Halperin et al note that LRYGB surgery may be useful in managing type 2 diabetes in patients with less severe obesity (BMI 30-42 kg/m^2). Schauer et al (2017) concluded that their results were consistent with other findings that surgical patients with lower BMIs of 27 kg/m^2 to 34 kg/m^2 and with diabetes had similar improvement in glycaemic control to patients who had a BMI of 35 kg/m^2 and above and this was superior to those who received medical therapy alone.

As noted by NICE in its guidance for preventing ill health and premature death in black, Asian and other minority ethnic groups, these groups are at an equivalent risk of diabetes, other health conditions or mortality at a lower BMI than the white European population [12]. Because of this, it may prove prudent to examine the possibility of providing weight loss interventions to these groups at a lower threshold BMI value than is currently used for the general population.

Bariatric surgery may be more cost effective in patients with a higher BMI.

While there is evidence to suggest that bariatric surgery is more cost effective in patients with a higher BMI, due to their increased capacity to gain through greater weight loss or resolution of existing co-morbidities, we found no evidence to suggest higher clinical effectiveness or safety of bariatric surgical procedures in patients with a higher baseline BMI.

For all procedure types in the 2014 UK National Bariatric Surgery Registry report [22], the percentage excess weight lost was inversely proportional to the baseline BMI. In other words, a greater proportion of their excess weight was lost by patients with lower baseline BMI. However, this may be a misleading target outcome. Moreover, caution must be taken with this Registry evidence, as the report was not a true controlled comparative study. Findings must be verified through formal randomised controlled trials (RCTs).

Cost effectiveness is highly dependent on the avoidance of costs associated with co-morbidities.

We did note that the cost effectiveness of bariatric surgery is very dependent upon the co-morbidity costs avoided. These costs may be avoided either from remission (temporary or otherwise) of an existing co-morbidity such as type 2 diabetes or reduction in incidence of obesity-related co-morbidities in the future. Obesity-related co-morbidities such as type 2 diabetes, hypertension or obstructive sleep apnoea, all require lifelong pharmacological and lifestyle management and are associated with additional complications (such as stroke, deep vein thrombosis, acute myocardial infarction, and amputation).

The difference in QALY gain between surgical and conservative treatment groups was very marginal [27, 56]. This means that bariatric surgery may be less cost effective if pharmacological management costs decrease or surgical costs increase (high complication / readmission rates, introduction of expensive instrumentation). Conversely, improvements in surgical outcomes which reduce complications and increase costs of conservative management (e.g. new drug costs or expensive new devices such as continuous glucose monitors) will lead to bariatric surgery being even more cost effective.

Patients with the greatest capacity to benefit are likely to be the most cost effective group to treat.

Given that cost effectiveness calculations factor in costs, effect size and the duration of effect, the cost per QALY is inherently biased toward patients who:

- Have the greatest capacity to benefit; and
- Have the potential to experience the benefit for a longer duration.

This means that from an economic perspective, bariatric surgery is likely to be most cost effective in patients who are:

- Younger or
- Have a higher BMI or
- Have an existing obesity-related co-morbidity which is likely to be resolved by significant weight loss resulting from bariatric surgery.

6 Search Strategy

Population	Intervention	Comparator	Outcomes	Studies
Adult patients with BMI ≥35 kg/m^2 with obesity-related co-morbidities or ≥40kg/m^2 without co-morbidity	Bariatric surgery (any technique)	Any non-surgical weight loss/weight management intervention	• Clinical effectiveness including ○ Resolution /remission of co-morbidities (e.g. hypertension, diabetes, reduced medication, improved glycaemic control) ○ BMI/weight reduction ○ Quality of life/patient-reported outcome measures • Safety/complications • Cost-effectiveness	• Meta-analyses • Systematic reviews • RCTs • Other controlled studies • Cohort studies • Case series (excluding single patient case reports) • Health economic analyses • Resource utilisation studies

Search Date: 22nd June 2017

Databases Searched: We searched Medline, Embase, Cochrane, TRIP and NICE Evidence search limited to July 2016 onwards and English language. Conference papers, letters, commentary and editorials were excluded. This rapid evidence review is an update of a full review undertaken in July 2016 when an identical search for evidence back to 2006 was undertaken.

Search string for TRIP and NICE

"bariatric surgery" OR "weight loss surgery" from:2016

Embase search

# ▲	Searches
1	morbid obesity/
2	((morbid* or extreme*) adj2 (obes* or overweight)).ti,ab.
3	((bmi or "body mass index") adj5 (35* or 40* or 45* or 50* or 55* or 60* or 65* or 70*)).ti,ab.
4	1 or 2 or 3
5	health promotion/ or health education/
6	social marketing/
7	counseling/
8	motivational interviewing/
9	(health promot* or health educat* or counsel* or motivational interview* or brief interview* or motivational advice or brief advice or brief intervention*).ti,ab.
10	((psycholog* or psychosocial or psycho-social or behavio?ral) adj3 (program* or service? or intervention?)).ti,ab.
11	5 or 6 or 7 or 8 or 9 or 10
12	exp kinesiotherapy/
13	exp exercise/

14	exp physical activity/
15	eating habit/
16	exp diet therapy/
17	lifestyle/
18	(diet* or nutrition* or healthy eating or healthful eating or eating healthily or healthy lifestyle).ti.
19	(physical activity or exercise? or active lifestyle or walk* or cycl* or run* or jog*).ti.
20	body weight management/
21	weight reduction/
22	((weight or bmi or body mass index) and (loss or lose or lost or losing or manage* or chang* or reduc*)).ti.
23	12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24	4 and 11 and 23
25	nutritional counseling/
26	lifestyle modification/
27	weight loss program/
28	((diet* or nutrition* or healthy eating or healthful eating or eating healthily or healthy lifestyle) adj5 (counsel* or advice* or support or promot*)).ti,ab.
29	((diet* or nutrition* or healthy eating or healthful eating or eating healthily or healthy lifestyle) adj5 (program* or service? or intervention*)).ti,ab.
30	((physical activity or exercise? or active lifestyle or walk* or cycl* or run* or jog*) adj5 (counsel* or advice* or support or promot*)).ti,ab.
31	((physical activity or exercise? or active lifestyle or walk* or cycl* or run* or jog*) adj5 (program* or service? or intervention*)).ti,ab.
32	((weight loss or weight management or weight reduction or weight change*) adj5 (counsel* or advice* or support or promot*)).ti,ab.
33	((weight loss or weight management or weight reduction or weight change*) adj5 (program* or service? or intervention*)).ti,ab.
34	((lifestyle or life style) adj5 (counsel* or advice* or support or promot*)).ti,ab.
35	((lifestyle or life style) adj5 (program* or service? or intervention*)).ti,ab.
36	((conventional or standard or medical or nonsurg* or non-surg*) adj2 (therap* or treatment or manage* or intervention?)).ti,ab.
37	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
38	4 and 37
39	exp bariatric surgery/
40	(bariatric surg* or weight loss surg*).ti,ab.
41	((gastric or intragastric or intra-gastric) adj2 (bypass* or band* or plication)).ti,ab.
42	(sleeve adj2 (gastrectomy or gastrectomies)).ti,ab.
43	((roux or jejuno* or ileal) adj3 bypass*).ti,ab.
44	((biliopancrea* or bilio-pancrea*) adj2 (diversion or bypass*)).ti,ab.
45	39 or 40 or 41 or 42 or 43 or 44
46	38 and 45
47	(2016* or 2017*).dp,dc,yr.
48	46 and 47
49	limit 48 to english language

50	conference*.pt.
51	49 not 50
52	4 and 45
53	47 and 52
54	limit 53 to "reviews (maximizes specificity)"
55	limit 54 to english language
56	55 not 50
57	51 or 56

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8 Clinician comments after 3 week consultation of the draft evidence review

The consultation period was from the 25th September to the 13th October.

No comments were received. The invitation to comment is below.

From: Barker Rachael (SPH)
Sent: 25 September 2017 16:08
To: 'martin.richardson@heartofengland.nhs.uk'; 'andrew.mckirgan@uhb.nhs.uk'; 'david.rosser@uhb.nhs.uk'; 'amir.khan@walsallhealthcare.nhs.uk'
Subject: BSOL CCGs Review of Bariatric Surgery
Importance: High

Subject: Solihull, Birmingham Cross City and Birmingham South Central CCGs Review of Bariatric Surgery

FAO: Clinicians with an interest in bariatric surgery in the CCG areas

Deadline for submission of comments: 5pm, Friday 13th October

Dear Colleagues,

Solihull, Birmingham Cross City and Birmingham South Central CCGs have commissioned Solutions for Public Health to produce a rapid evidence review on the clinical and cost effectiveness of bariatric surgery compared with non-surgical management.

This review will be considered by CCGs Treatment Policies Clinical Review Group and will inform future commissioning policy.

We have been given your name by the CCGs and we would be very grateful if you would consider either commenting on the attached review or passing it on to an appropriate colleague.

Please do not circulate this draft review beyond your NHS Trust or organisation (including posting to websites) or pass on to individual patients or patient groups as the CCG process does not include patient and public consultation at this draft stage.

In particular, we are keen to receive comments on the following:

1. **Evidence review**

   - Have we included all relevant studies?
   - Have we summarised and appraised the evidence appropriately?

   Please note that the CCGs do not consider evidence from conference posters and abstracts as the information is insufficient for critical appraisal.

2. **Current CCG activity and clinical practice**
   - Is the activity data presented an accurate reflection of current activity?
   - Are you aware of any additional issues which should be taken into account e.g. problems with IFR authorisation, routine coding, recent changes in clinical practice which would render the information out of date, etc? Please provide details.

- Do you have any additional information which should be considered e.g. your local pathways/protocols; audit results, national standards etc?

3. **Clinical opinion**

The CCGs value the opinion of specialist clinicians. This could include:

- Your view of the likely benefit of the procedure in practice;
- Where you feel the intervention should fit within the care pathway (including any criteria for access which you either currently use or would like to see in place);
- The number of patients you consider would benefit from access to the intervention across Solihull, Birmingham Cross City and Birmingham South Central CCGs.

4. **Format for Comments**

Your response should be submitted **in writing by 5pm, Friday 13th October**, preferably sent electronically in Word format or as an email text. We will include all written responses received in the appendix of the evidence review document. The main purpose of the review is to provide an evidence base for discussion by the CCGs Health Policy Committee. Although not a public document, your comments may be available to a wider audience, and may be subject to FOI request.

5. Finally, the CCGs may wish to invite lead clinicians to attend the CCGs Treatment Policies Clinical Review Group to contribute their advice and expertise to the CCGs discussion. The CCGs Treatment Policies Review Group meeting will be on Thursday 2nd November, at Friars Gate from 1.30-3.30pm. If would like to attend please contact Terri-Ann Millington (terri-ann.millington@nhs.net) who will register your interest and provide further details on specific agenda timings.

Please note that CCGs regard it as very important that all information on each topic is circulated in advance of the meetings. You will not have the opportunity to make a formal presentation or table new material at the meeting. May I therefore stress that it is very important that we receive your written input in advance.

We look forward to hearing from you and thank you in advance for your input to this.

Competing Interest

All SPH authors have completed the ICMJE uniform disclosure form (www.icmje.org/coi_disclosure.pdf) and declare: grants from Solihull CCG, Birmingham CrossCity CCG and Birmingham South Central CCG to SPH to undertake the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years and no other relationships or activities that could appear to have influenced the submitted work.

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Appendix 1 – Levels of Evidence

Oxford Centre for Evidence-based Medicine – Levels of Evidence (March 2009)[4]

The CEBM ‘Levels of Evidence 1’ document sets out one approach to systematising this process for different question types (see our glossary).

Level	Therapy / Prevention, Aetiology / Harm	Prognosis	Diagnosis	Differential diagnosis / symptom prevalence study	Economic and decision analyses
1a	SR (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR” validated in different populations	SR (with homogeneity*) of Level 1 diagnostic studies; CDR” with 1b studies from different clinical centres	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of Level 1 economic studies
1b	Individual RCT (with narrow Confidence Interval”¡)	Individual inception cohort study with > 80% follow-up; CDR” validated in a single population	Validating** cohort study with good” ” ” reference standards; or CDR” tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
1c	All or none§	All or none case-series	Absolute SpPins and SnNouts” “	All or none case-series	Absolute better-value or worse-value analyses ” ” ” “
2a	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of Level >2 diagnostic studies	SR (with homogeneity*) of 2b and better studies	SR (with homogeneity*) of Level >2 economic studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-	Retrospective cohort study or follow-up of untreated control patients in an RCT;	Exploratory** cohort study with good” ” ” reference standards; CDR” after derivation, or	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited

[4] Produced by Bob Phillips, Chris Ball, Dave Sackett, Doug Badenoch, Sharon Straus, Brian Haynes, Martin Dawes since November 1998. Updated by Jeremy Howick March 2009.

	up)	Derivation of CDR" or validated on split-sample§§§ only	validated only on split-sample§§§ or databases		review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
3a	SR (with homogeneity*) of case-control studies		SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
4	Case-series (and poor quality cohort and case-control studies§§)	Case-series (and poor quality prognostic cohort studies***)	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

Notes: Users can add a minus-sign "-" to denote the level of that fails to provide a conclusive answer because:

- ***EITHER*** a single result with a wide Confidence Interval
- ***OR*** a Systematic Review with troublesome heterogeneity.

Such evidence is inconclusive, and therefore can only generate Grade D recommendations.

*	By homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.
"	Clinical Decision Rule. (These are algorithms or scoring systems that lead to a prognostic estimation or a diagnostic category.)

“¡	See note above for advice on how to understand, rate and use trials or other studies with wide confidence intervals.
§	Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it.
§§	By poor quality cohort study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and non-exposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor quality case-control study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls and/or failed to identify or appropriately control known confounders.
§§§	Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into “derivation” and “validation” samples.
” “	An “Absolute SpPin” is a diagnostic finding whose Specificity is so high that a Positive result rules-in the diagnosis. An “Absolute SnNout” is a diagnostic finding whose Sensitivity is so high that a Negative result rules-out the diagnosis.
“¡”¡	Good, better, bad and worse refer to the comparisons between treatments in terms of their clinical risks and benefits.
” ” “	Good reference standards are independent of the test, and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a non-independent reference standard (where the ‘test’ is included in the ‘reference’, or where the ‘testing’ affects the ‘reference’) implies a level 4 study.
” ” ” “	Better-value treatments are clearly as good but cheaper, or better at the same or reduced cost. Worse-value treatments are as good and more expensive, or worse and the equally or more expensive.
**	Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g. using a regression analysis) to find which factors are ‘significant’.
***	By poor quality prognostic cohort study we mean one in which sampling was biased in favour of patients who already had the target outcome, or the measurement of outcomes was accomplished in <80% of study patients, or outcomes were determined in an unblinded, non-objective way, or there was no correction for confounding factors.
****	Good follow-up in a differential diagnosis study is >80%, with adequate time for alternative diagnoses to emerge (for example 1-6 months acute, 1 – 5 years chronic)

Appendix 2 - Abbreviations

- **ADL** .... activities of daily living
- **AGB** .... adjustable gastric band
- **BDDS** .... biliopancreatic diversion with duodenal switch
- **BMI** .... body mass index
- **BP** .... blood pressure
- **CI** .... confidence interval
- **GORD** .... gastro-oesophageal reflux disease
- **HbA1c** .... glycated haemoglobin (provides an overall picture of average blood sugar levels over a period of weeks/months)
- **HDL** .... high-density lipoprotein
- **HR** .... hazard ratio
- **I^2** .... a measure of heterogeneity of studies in the meta-analysis. The Cochrane Handbook suggests where I2<40%, heterogeneity is unlikely to be important.
- **ICER** .... incremental cost-effectiveness ratio
- **ICU** .... intensive care unit
- **ILMI** .... Intensive Lifestyle and Medical Intervention
- **Lap** .... laparoscopic
- **LDL** .... low-density lipoprotein
- **LSG** .... Laparoscopic sleeve gastrectomy
- **LOS** .... length of stay
- **LRYGB** .... Laparoscopic Roux-en-Y gastric bypass
- **MO** .... morbid obesity
- **OR** .... odds ratio
- **OSA** .... obstructive sleep apnoea
- **p.a.** .... per annum
- **QALY** .... quality-adjusted life year
- **QoL** .... quality of life
- **RR** .... risk ratio
- **RYGB** .... Roux-en-Y gastric bypass
- **SG** .... sleeve gastrectomy
- **T2DM** .... type 2 diabetes mellitus
- **TG** .... triglycerides