National Clinical Guideline Centre

Obesity

Identification, assessment and management of overweight and obesity in children, young people and adults

Partial update of CG43

Methods, evidence and recommendations

November 2014

Commissioned by the National Institute for Health and Care Excellence

Funding
National Institute for Health and Care Excellence

Update information

July 2023: NICE's original guideline on obesity was published in 2014. Section 1.10 on surgical interventions has been amended by the 2023 update after reviewing evidence on bariatric surgery for people living with overweight and obesity.

See the NICE website for the guideline recommendations and the evidence review for the 2023 update. This document preserves evidence reviews and committee discussions for areas of the guideline that were not updated in 2023.

September 2022: We updated the recommendations on identification and classification of overweight and obesity from NICE guideline CG189 and added recommendations from PH46. The new recommendations replace sections 8.2, 8.3 and 8.4 in this document. We also added new recommendations for research.

Minor changes since publication

April 2023: We updated the section on pharmacological interventions to include recommendations from NICE technology appraisal guidance on liraglutide, semaglutide and naltrexone–bupropion.

February 2021 We updated the information on recommended amounts of exercise in in line with the 2019 UK Chief Medical Officers' physical activity guidelines.

Contents

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Acknowledgements

The Guideline development group and project team would like to thank Katie Broomfield, Tamara Diaz, Stacey Martin, Jacoby Patterson, Nancy Turnbull, Maggie Westby, Carlos Sharpin, Liz Rouncefield and Alex Allen for all their help and support throughout the guideline.

Guideline update

The guidance is a partial update of NICE clinical guideline 43 (published December 2006). NICE has a suite of guidance on obesity including the following guidance: PH27 Weight management before, during and after pregnancy (July 2010), PH42 Obesity – working with local communities (November 2012), PH46 Body mass index and waist circumference thresholds for intervening to prevent ill health among black, Asian and other minority ethnic groups (June 2013), PH44 Overweight and obese adults – lifestyle management (May 2014), PH47 Managing overweight and obesity among children and young people (October 2013), PH49 Behaviour change – individual approaches (January 2014), PH53 Managing overweight and obesity in adults – lifestyle weight management services (May 2014) and Maintaining a healthy weight and preventing excess weight gain among children and adults (due to be published in February 2015). Maintaining a healthy weight and preventing excess weight gain among children and adults will replace clinical section 1.1.1 in CG43. NICE have developed an Obesity pathway which will link all obesity-related guidance, and have developed a related pathway on physical activity.

New and updated recommendations have been included covering very-low-calorie diets, bariatric surgery in people with recent-onset type 2 diabetes and follow-up care after bariatric surgery.

Recommendations are marked to indicated the year of the last evidence review [2014] if the evidence has not been updated since the original guideline, [2006, amended 2014] if the evidence has not been updated since the original guideline, but changes have been made that alter the meaning of the recommendation, [2014] if the evidence has been reviewed but no change has been made to the recommendation and [new 2014] if the evidence review has been added or updated.

The original NICE guidance and supporting documents are available from https://www.nice.org.uk/guidance/cg43.

Appendices M, N and P contain all the evidence and discussion that underpinned the original CG43 recommendations that are included in this guideline. Only evidence for the new reviews is contained within this document.

2 Introduction

Overweight and obesity are increasing problems that lead to significant health and social difficulties for people. Commonly defined by a measurement of Body Mass Index (BMI - calculated by dividing body weight (kilograms) by height (metres) squared), the prevalence of overweight (adult BMI of between 25 and 29.9) and obesity (BMI of 30 or over) is increasing. For children, these BMI standards require adjustments for age and gender. Overweight and obesity are global problems and the World Health Organization (WHO) predicts that by 2015 approximately 2.3 billion adults worldwide will be overweight and more than 700 million obese. In the UK, obesity rates have nearly doubled in the past 18 years from 13% of men and 16% of women in 1993, to 24% of men and 26% of women in 2011. In the same year, about 3 in 10 children aged 2–15 years were found to be overweight or obese. Ethnic differences exist in the prevalence of obesity and the related risk of ill health. For example, compared with the general population, the prevalence of obesity is lower in men of Bangladeshi and Chinese family origin, whereas it is higher for women of African, Caribbean and Pakistani family origin as reported by the National Obesity Observatory in 2011.

Obesity is directly linked to a number of different illnesses including type 2 diabetes, hypertension, gallstones and gastro-oesophageal reflux disease, as well as psychological and psychiatric morbidities. The Health and Social Care Information Centre reported that there were 11,740 inpatient admissions to hospitals in England with a primary diagnosis of obesity in 2011/2012, which is 3 times as many as 5 years earlier in 2006/2007. There were 3 times as many women admitted as men.

The cost of overweight and obesity to society and the economy was estimated to be almost £16 billion in 2007 (over 1% of gross domestic product). The cost could increase to just under £50 billion in 2050 if obesity rates continue to rise, according to projections from the Department of Health. A simulated model reported in the Lancet predicted that there would be 11 million more obese adults in the UK by 2030, with combined medical costs for treatment of associated diseases estimated to increase by £1.9–2 billion/year.

Treatment options for obesity may include non-surgical treatment and bariatric surgery. Non-surgical treatment usually takes a multicomponent approach, involving dietary changes to reduce calorie intake, an increase in physical activity, behavioural modification, and where appropriate, psychological support or pharmacotherapy.

NICE issued guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children in 2006 (CG43). This was a joint clinical and public health guideline developed by the National Collaborating Centre for Primary Care (now merged as part of the National Clinical Guidelines Centre) and NICE's Centre for Public Health Excellence. Despite the guidance, there remain significant variations in existing service provision for people with obesity and, in many places, the multicomponent programmes that are required for both prevention and treatment are limited. The 2013 Royal College of Physicians report 'Action on obesity: comprehensive care for all' reported that access to surgery for obesity in some areas of the UK did not reflect the guideline recommendations.

The 2006 guideline was reviewed for update in 2011, leading to this partial update. This guideline addresses 3 main areas - follow-up care packages after bariatric surgery; the role of bariatric surgery in the management of recent-onset type 2 diabetes; very-low-calorie diets including their effectiveness, safety and effective management strategies for maintaining weight loss after such diets.

The public health aspects of CG43 are not addressed here, but are in the process of being updated by the Centre for Public Health Excellence. The public health recommendations that formed part of CG43 will continue to exist within the original piece of guidance. All other clinical recommendations from areas not subject to update have been reviewed to ensure that they comply with the NICE

policy on non-discrimination and, where appropriate, have been amended or the wording changed in line with current NICE house style (see Section 3.1).

3 Development of the guideline

3.1 What is a NICE clinical guideline?

NICE clinical guidelines are recommendations for the care of individuals in specific clinical conditions or circumstances within the NHS – from prevention and self-care through primary and secondary care to more specialised services. We base our clinical guidelines on the best available research evidence, with the aim of improving the quality of health care. We use predetermined and systematic methods to identify and evaluate the evidence relating to specific review questions.

NICE clinical guidelines can:

- provide recommendations for the treatment and care of people by health professionals
- be used to develop standards to assess the clinical practice of individual health professionals
- be used in the education and training of health professionals
- help patients to make informed decisions
- improve communication between patient and health professional.

While guidelines assist the practice of healthcare professionals, they do not replace their knowledge and skills.

We produce our guidelines using the following steps:

- Guideline topic is referred to NICE from the Department of Health.
- Stakeholders register an interest in the guideline and are consulted throughout the development process.
- The scope is prepared by the National Clinical Guideline Centre (NCGC).
- The NCGC establishes a Guideline Development Group.
- A draft guideline is produced after the group assesses the available evidence and makes recommendations.
- There is a consultation on the draft guideline.
- The final guideline is produced.

The NCGC and NICE produce a number of versions of this guideline:

- the 'full guideline' contains all the recommendations, plus details of the methods used and the underpinning evidence
- the 'NICE guideline' lists the recommendations
- 'information for the public' is written using suitable language for people without specialist medical knowledge
- NICE Pathways brings together all connected NICE guidance.

This version is the full version. The other versions can be downloaded from NICE at www.nice.org.uk.

3.2 Remit

This is a partial update of Obesity (NICE clinical guideline 43). See Appendix A for details of which sections will be updated.

An editorial review of all recommendations has also been carried out, for example to ensure that they comply with NICE's duties under equalities legislation.

This update is being undertaken as part of the guideline review cycle.

3.3 Who developed this guideline?

A multidisciplinary Guideline Development Group (GDG) comprising health professionals and researches as well as lay members developed this guideline (see the list of Guideline Development Group members and the acknowledgements).

The National Institute for Health and Care Excellence (NICE) funds the National Clinical Guideline Centre (NCGC) and thus supported the development of this guideline. The GDG was convened by the NCGC and chaired by Dr Peter Barry in accordance with guidance from NICE.

The group met every 4 weeks during the development of the guideline. At the start of the guideline development process all GDG members declared interests including consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared arising conflicts of interest.

Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix B.

Staff from the NCGC provided methodological support and guidance for the development process. The team working on the guideline included a project manager, systematic reviewers, health economists and information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate and drafted the guideline in collaboration with the GDG.

(a) What this guideline covers

The guideline covers the following populations:

- Adults, children and young people (aged 2 years and older) who are overweight and obese. This includes those with established comorbidities, and those with or without risk factors for other medical conditions.
- The following special groups, which have high rates of morbidity caused by obesity, will be considered when there is good evidence of effectiveness of separate interventions targeted at these groups:
  - black and minority ethnic groups
  - people from lower socioeconomic groups
  - young people
  - people with learning disabilities
  - older people
  - people with type 2 diabetes.

For further details please refer to the scope in Appendix A and review questions in Section 6.1.

(b) What this guideline does not cover

The guideline does not cover people of a healthy weight, pregnant women or children under 2 years of age.

Relationships between the guideline and other NICE guidance

Related NICE Interventional procedures guidance:

- Laparoscopic gastric plication for the treatment of severe obesity. NICE interventional procedure guidance 432 (2012)

Related NICE Clinical guidelines:

- Gallstone disease. NICE clinical guideline XXX (2014).
- Dyspepsia and gastro-oesophageal reflux disease: Investigation and management of dyspepsia, symptoms suggestive of gasto-oesophageal reflux disease, or both. NICE clinical guideline 184 (2014).
- Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. NICE clinical guideline 181 (2014).
- Patient experience in NHS services. NICE clinical guideline 138 (2012)
- Medicines adherence. NICE clinical guideline 76 (2009)
- Type 2 diabetes: the management of type 2 diabetes. NICE clinical guidance 87 (2009)
- Eating disorders. NICE clinical guideline 9 (2004)
- Preoperative tests. NICE clinical guideline 3 (2003)

Related NICE Public health guidance:

- Exercise referral schemes to promote physical activity. NICE public health guidance 54 (2014).
- Overweight and obese adults: lifestyle weight management services. NICE public health guidance 53 (2014)
- Behaviour change: individual approaches. NICE public health guidance 49 (2014)
- Managing overweight and obesity among children and young people. NICE public health guidance 47 (2013)
- Assessing body mass index and waist circumference thresholds for intervening to prevent ill health and premature death among adults from black, Asian and other minority ethnic groups in the UK. NICE public health guidance 46 (2013)
- Physical activity: brief advice for adults in primary care. NICE public health guidance 44 (2013). Obesity: working with local communities. NICE public health guidance 42 (2012).
- Preventing type 2 diabetes: risk identification and interventions for individuals at high risk. NICE public health guidance 38 (2012).
- Walking and cycling. NICE public health guidance 41 (2012).
- Preventing type 2 diabetes: population and community level interventions. NICE public health guidance 35 (2011).
- Prevention of cardiovascular disease. NICE public health guidance 25 (2010).
- Weight management before, during and after pregnancy. NICE public health guidance 27 (2010).
- Promoting physical activity for children and young people. NICE public health guidance 17 (2009).
- Maternal and child nutrition. NICE public health guidance 11 (2008).
- Four commonly used methods to increase physical activity. NICE public health guidance 2 (2006).

Related NICE guidance currently in development:

- Liver disease (non-alcoholic fatty [NAFLD]). NICE clinical guideline. Publication expected TBC.
- Maintaining a healthy weight and preventing excess weight gain among children and adults. NICE public health guidance. Publication expected March 2015.
- Type 2 diabetes in adults (update). NICE clinical guideline. Publication expected August 2015.

4 Methods

This chapter sets out in detail the methods used to review the evidence and to generate the recommendations that are presented in subsequent chapters. This guidance was developed in accordance with the methods outlined in the NICE guidelines manual 2012[44].

4.1 Amendments to 2006 text

All text and recommendations from the previous guideline, CG43, that has not been updated (therefore review questions have not been generated and evidence has not been searched for) has been left unchanged. Amendments to recommendations are detailed in Appendix Q.

4.2 Developing the review questions and outcomes

Review questions were developed in a PICO framework (patient, intervention, comparison and outcome) for intervention reviews.

This use of a framework guided the literature searching process, critical appraisal and synthesis of evidence, and facilitated the development of recommendations by the Guideline Development Group (GDG). The review questions were drafted by the NCGC technical team and refined and validated by the GDG. The questions were based on the key clinical areas identified in the scope (Appendix A).

A total of 5 review questions were identified.

Full literature searches, critical appraisals and evidence reviews were completed for all the specified review questions.

Table 1: Review questions

Chapter	Type of review	Review questions	Outcomes
6	Intervention	In people who are overweight or obese, what is the clinical and cost effectiveness of very-low-calorie diets (VLCD) in reducing weight?	**Critical outcomes:** • % weight change (kg) at final end score • Health related quality of life • Withdrawals **Important outcomes:** • BMI final score compared to start - % reduction • Weight change at end of VLCD to end of study - % kg • Weight change at end of diet to end of study - % BMI • Improvement in physical activity
6	Intervention	In people who are overweight or obese, what is the safety of VLCD when used to reduce and maintain weight loss?	**Critical outcomes:** • Disordered eating • Depression score • Postural hypotension **Important outcomes:** • Bone density • Constipation

Chapter	Type of review	Review questions	Outcomes
			• Gallstones • Gout • Diarrhoea • Hypoglycaemia
6	Intervention	What are effective management strategies for maintaining weight loss after VLCD in people who are overweight or obese?	Critical outcomes: • % weight change (kg) from end of VLCD to end of study • Health related quality of life • Dropouts Important outcomes: • % weight change (BMI) from end of VLCD to end of study • % weight change from before VLCD to end of study (kg) • % weight change from before VLCD to end of study (BMI) • Improvement in physical activity
7	Intervention	In people with recent-onset type 2 diabetes (T2D) who are also overweight and obese, what is the clinical and cost effectiveness of bariatric surgery for the management of diabetes?	**Critical outcomes:** • % weight change (BMI or kg) • Improvement (glycaemic control) • Health related quality of life **Important outcomes:** • Remission of type 2 diabetes • Mortality • Weight in BMI • Weight in kg • Reduction of diabetic medication
8	Intervention	What is the clinical and cost effectiveness to follow-up care packages after bariatric surgery compared with usual care?	**Critical outcomes:** • % weight loss at end of study • Development of at least 1 micronutrient deficiency • Health related quality of life **Important outcomes:** • Reoperation rate • Mortality • Reduction in medication use • Psychological well-being

4.3 Searching for evidence

4.3.1 Clinical literature search

Systematic literature searches were undertaken to systematically identify all published clinical evidence relevant to the review questions. Searches were undertaken according to the parameters stipulated within The guidelines manual 2012.[44] Databases were searched using relevant medical subject headings, free-text terms and study-type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English. All searches were conducted in MEDLINE, Embase, and The Cochrane Library. In addition, PsycINFO was used for the questions on very-low-calorie diets and care packages after bariatric surgery.

Search strategies were quality assured by cross-checking reference lists of highly relevant papers, analysing search strategies in other systematic reviews, and asking GDG members to highlight any additional studies. The questions, the study types applied, the databases searched and the years covered can be found in Appendix F.

The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were assessed against the inclusion criteria.

4.3.2 Health economic literature search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting searches using the population and intervention terms in the NHS Economic Evaluation Database (NHS EED), the Health Technology Assessment database (HTA) and the Health Economic Evaluations Database (HEED) from 2006 onwards. Additionally, the search was run on MEDLINE and Embase using a specific economic filter, population and intervention terms, from 2006, to ensure recent publications that had not yet been indexed by the economic databases were identified. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English.

The health economic search strategies are included in Appendix F.

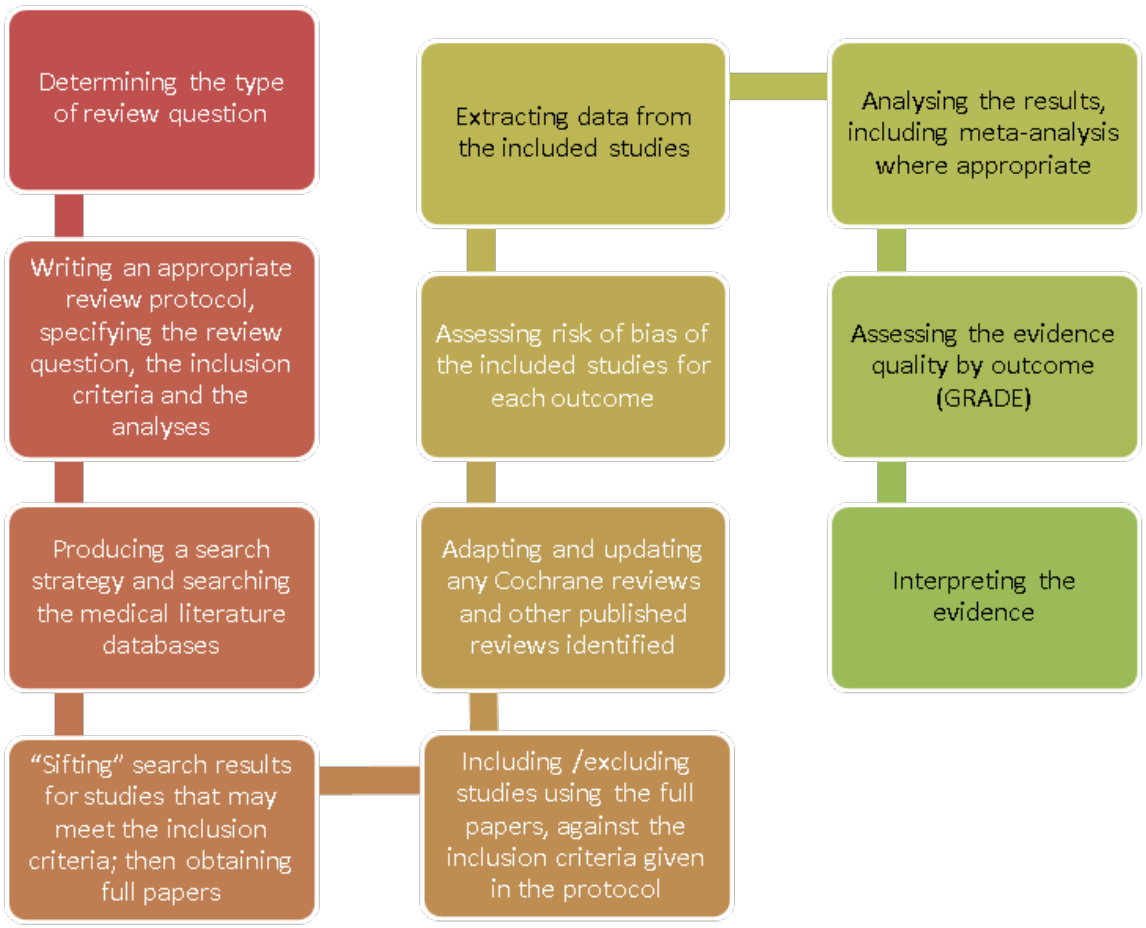
4.4 Evidence of effectiveness

The evidence was reviewed following the steps shown schematically in Figure 1:

- Potentially relevant studies were identified for each review question from the relevant search results by reviewing titles and abstracts. Full papers were then obtained.
- Full papers were reviewed against pre-specified inclusion and exclusion criteria to identify studies that addressed the review question in the appropriate population (review protocols are included in Appendix C).
- Relevant studies were critically appraised using the appropriate checklist as specified in The guidelines manual.[44]
- Key information was extracted on the study's methods, PICO factors and results. These were presented in summary tables (in each review chapter) and evidence tables (in Appendix G).
- Summaries of evidence were generated by outcome (included in the relevant review chapters) and were presented in GDG meetings:
    - Randomised studies: data were meta-analysed where appropriate and reported in GRADE profiles (for intervention reviews).

A sample of the above stages of the reviewing process was quality assured by a second reviewer to eliminate any potential of reviewer bias or error.

Figure 1: Step-by-step process of review of evidence in the guideline



4.4.1 Inclusion and exclusion criteria

The inclusion and exclusion of studies was based on the review protocols, which can be found in Appendix C. Excluded studies by review question (with the reasons for their exclusion) are listed in Appendix J. The GDG was consulted about any uncertainty regarding inclusion or exclusion.

The guideline population was people who are overweight defined as a BMI 25-29.9 (kg/m^2) or obese defined as a BMI 30 or over (kg/m^2). The review population included adults and children over 2 years old. The only exception was for the question on follow-up care packages after bariatric surgery which included adults and young people (post puberty) as prepuberty children would need different follow-up care.

For the review question on bariatric surgery in type 2 diabetes, the review population included overweight and obese adults with recent-onset type 2 diabetes. Recent-onset type 2 diabetes was defined as a duration of less than or equal to 10 years.

Literature reviews, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

The review protocols are presented in Appendix C.

4.4.2 Methods of combining clinical studies

4.4.2.1 Data synthesis for intervention reviews

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software. Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for the binary outcomes: reoperation rate, mortality, remission of type 2 diabetes, reduction of diabetic medication, withdrawals, depression tendencies, constipation, gallstones and diarrhoea.

For continuous outcomes, measures of central tendency (mean) and variation (standard deviation) were required for meta-analysis. Data for continuous outcomes [% weight change (kg or BMI), weight change (kg or BMI), improvement in glycaemic control, use of diabetic medication, health related quality of life, psychological well-being, improvement in physical activity, depression score and binge eating] were analysed using an inverse variance method for pooling weighted mean differences and, where the studies had different scales, standardised mean differences were used. A generic inverse variance option in RevMan5 was used if any studies reported solely the summary statistics and 95% confidence interval (95% CI) or standard error; this included any hazard ratios reported. However, in cases where standard deviations were not reported per intervention group, the standard error (SE) for the mean difference was calculated from other reported statistics (p values or 95% CIs); meta-analysis was then undertaken for the mean difference and SE using the generic inverse variance method in RevMan5. When the only evidence was based on studies that summarised results by presenting medians (and interquartile ranges), or only p values were given, this information was assessed in terms of the study's sample size and was included in the GRADE tables without calculating the relative or absolute effects. Consequently, aspects of quality assessment such as imprecision of effect could not be assessed for evidence of this type.

When reported time to event data was presented as a hazard ratio.

Stratified analyses were predefined for the review questions at the protocol stage when the GDG identified that these strata are different in terms of biological and clinical characteristics and the interventions were expected to have a different effect on subpopulations. Strata included:

- Different BMI categories
- People with learning disabilities
- Young people (puberty onwards)

For more information on strata refer to the protocols (see Appendix C).

Statistical heterogeneity was assessed by visually examining the forest plots, and by considering the chi-squared test for significance at $p<0.1$ or an I-squared inconsistency statistic (with an I-squared value of more than 50% indicating considerable heterogeneity). Where considerable heterogeneity was present, we carried out predefined subgroup analyses detailed in the protocols (see Appendix C).

Assessments of potential differences in effect between subgroups were based on the chi-squared tests for heterogeneity statistics between subgroups. If no sensitivity analysis was found to completely resolve statistical heterogeneity then a random-effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect.

The means and standard deviations of continuous outcomes were required for meta-analysis. However, in cases where standard deviations were not reported, the standard error was calculated if the p values or 95% CIs were reported and meta-analysis was undertaken with the mean and standard error using the generic inverse variance method in RevMan5. Where p values were reported as 'less than', a conservative approach was undertaken. For example, if p value was reported as '$p\leq0.001$', the calculations for standard deviations will be based on a p value of 0.001. If

these statistical measures were not available then the methods described in Section 16.1.3 of the Cochrane Handbook (September 2009) 'Missing standard deviations' were applied as the last resort.

For interpretation of the binary outcome results, differences in the absolute event rate were calculated using the GRADEpro software, for the median event rate across the control arms of the individual studies in the meta-analysis. Absolute risk differences were presented in the GRADE profiles and in clinical summary of findings tables, for discussion with the GDG.

For binary outcomes, absolute event rates were also calculated using the GRADEpro software using event rate in the control arm of the pooled results.

4.4.3 Type of studies

For most intervention reviews in this guideline, parallel randomised controlled trials (RCTs) were included because they are considered the most robust type of study design that could produce an unbiased estimate of the intervention effects. If there was limited evidence from RCTs, a conference abstract search was completed and authors were contacted for further information of any relevant studies. Please refer to Appendix C for full details on the study design of studies selected for each review question.

4.4.4 Appraising the quality of evidence by outcomes

The evidence for outcomes from the included RCTs and, where appropriate, observational studies were evaluated and presented using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group (http://www.gradeworkinggroup.org/). The software developed by the GRADE working group (GRADEpro) was used to assess the quality of each outcome, taking into account individual study quality factors and the meta-analysis results. Results were presented in GRADE profiles ('GRADE tables'), which consist of 2 sections: the 'Clinical evidence profile' table includes details of the quality assessment while the 'Clinical evidence summary of findings' table includes pooled outcome data, where appropriate, an absolute measure of intervention effect and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate summary measures and measures of dispersion (such as mean and standard deviation or median and range) for continuous outcomes and frequency of events (n/N: the sum across studies of the number of patients with events divided by sum of the number of completers) for binary outcomes.

The evidence for each outcome was examined separately for the quality elements listed and defined in Table 2. Each element was graded using the quality levels listed in Table 3. The main criteria considered in the rating of these elements are discussed below (see Section 6.4.5 Grading of evidence). Footnotes were used to describe reasons for grading a quality element as having serious or very serious problems. The ratings for each component were summed to obtain an overall assessment for each outcome (Table 4).

Table 2: Description of the elements in GRADE used to assess the quality of intervention studies

Quality element	Description
Risk of bias ('Study limitations')	Limitations in the study design and implementation may bias the estimates of the treatment effect. High risk of bias for the majority of the evidence decreases confidence in the estimate of the effect
Inconsistency	Inconsistency refers to an unexplained heterogeneity of results
Indirectness	Indirectness refers to differences in study population, intervention, comparator and outcomes between the available evidence and the review question, or recommendation made, such that the effect estimate is changed
Imprecision	Results are imprecise when studies include relatively few patients and few events and

Quality element	Description
	thus have wide confidence intervals around the estimate of the effect. Imprecision results if the confidence interval includes the clinically important threshold
Publication bias	Publication bias is a systematic underestimate or an overestimate of the underlying beneficial or harmful effect due to the selective publication of studies

Table 3: Levels of quality elements in GRADE

Level	Description
None	There are no serious issues with the evidence
Serious	The issues are serious enough to downgrade the outcome evidence by 1 level
Very serious	The issues are serious enough to downgrade the outcome evidence by 2 levels

Table 4: Overall quality of outcome evidence in GRADE

Level	Description
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

4.4.5 Grading the quality of clinical evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

1. A quality rating was assigned, based on the study design. RCTs start as High, observational studies as Low, and uncontrolled case series as Low or Very low.
2. The rating was then downgraded for the specified criteria: risk of bias (study limitations), inconsistency, indirectness, imprecision and publication bias. These criteria are detailed below. Evidence from observational studies (which had not previously been downgraded) was upgraded if there was: a large magnitude of effect, a dose–response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have 'serious' or 'very serious' risk of bias was rated down by 1 or 2 points respectively.
3. The downgraded or upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as High and the overall quality became Moderate, Low or Very low if 1, 2 or 3 points were deducted respectively.
4. The reasons or criteria used for downgrading were specified in the footnotes.

The details of the criteria used for each of the main quality element are discussed further in the following Sections 6.4.6 to 6.4.9.

4.4.6 Risk of bias

Bias can be defined as anything that causes a consistent deviation from the truth. Bias can be perceived as a systematic error, for example, multiple replications of the same study would reach the wrong answer on average.

The risk of bias for a given study and outcome is associated with the risk of over- or underestimation of the true effect.

The risks of bias are listed in Table 5.

A study with a poor methodological design does not automatically imply high risk of bias; the bias is considered individually for each outcome and it is assessed whether this poor design will impact on the estimation of the intervention effect.

Table 5: Risk of bias in randomised controlled trials

Risk of bias	Explanation
Allocation concealment	Those enrolling patients are aware of the group to which the next enrolled patient will be allocated (this is a major problem in 'pseudo' or 'quasi' randomised trials with, for example, allocation by day of week, birth date, chart number)
Lack of blinding	Patient, caregivers, those recording outcomes, those adjudicating outcomes, or data analysts are aware of the arm to which patients are allocated
Incomplete accounting of patients and outcome events	Missing data not accounted for and failure of the trialists to adhere to the intention-to-treat principle when indicated
Selective outcome reporting	Reporting of some outcomes and not others on the basis of the results
Other risks of bias	For example: • Stopping early for benefit observed in randomised trials, in particular in the absence of adequate stopping rules • Use of unvalidated patient-reported outcomes • Recruitment bias in cluster-randomised trials

4.4.7 Inconsistency

Inconsistency refers to an unexplained heterogeneity of results. When estimates of the treatment effect across studies differ widely (that is, there is heterogeneity or variability in results), this suggests true differences in underlying treatment effect.

Heterogeneity in meta-analyses was examined and sensitivity and subgroup analyses performed as pre-specified in the protocols (Appendix C).

When heterogeneity exists (chi-squared $p<0.1$, I-squared inconsistency statistic of over 50%, or evidence from examining forest plots), but no plausible explanation can be found (for example, duration of intervention or different follow-up periods), the quality of evidence was downgraded by 1 or 2 levels, depending on the extent of uncertainty to the results contributed by the inconsistency in the results. In addition to the I-squared and chi-squared values, the decision for downgrading was also dependent on factors such as whether the intervention is associated with benefit in all other outcomes or whether the uncertainty about the magnitude of benefit (or harm) of the outcome showing heterogeneity would influence the overall judgment about net benefit or harm (across all outcomes).

4.4.8 Indirectness

Directness refers to the extent to which the populations, intervention, comparisons and outcome measures are similar to those defined in the inclusion criteria for the reviews. Indirectness is important when these differences are expected to contribute to a difference in effect size, or may affect the balance of harms and benefits considered for an intervention. In the bariatric surgery review the population was overweight and obese people with recent-onset of type 2 diabetes

(duration equal to or less than 10 years). Studies that had a mean duration less than 10 years but with wide standard deviation (including some patients with duration over 10 years) were included in the review but downgraded for indirectness.

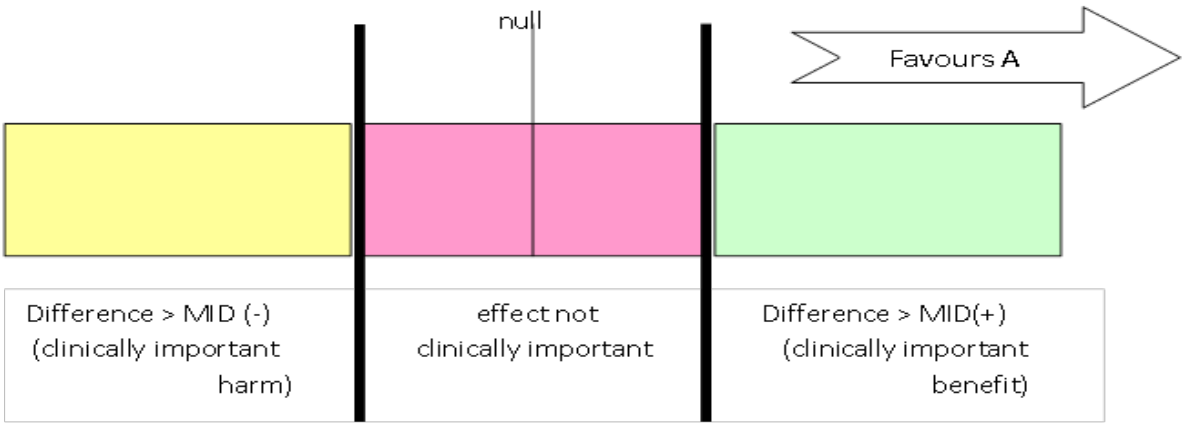
4.4.9 Imprecision

Imprecision in guidelines concerns whether the uncertainty (confidence interval) around the effect estimate means that it is not clear whether there is a clinically important difference between interventions or not. Therefore, imprecision differs from the other aspects of evidence quality in that it is not really concerned with whether the point estimate is accurate or correct (has internal or external validity); instead it is concerned with the uncertainty about what the point estimate is. This uncertainty is reflected in the width of the confidence interval.

The 95% confidence interval (95% CI) is defined as the range of values that contain the population value with 95% probability. The larger the trial, the smaller the 95% CI and the more certain the effect estimate.

Imprecision in the evidence reviews was assessed by considering whether the width of the 95% CI of the effect estimate is relevant to decision-making, considering each outcome in isolation. Figure 2: Illustration of precise and imprecise outcomes based on the confidence interval of outcomes in a forest plot considers a positive outcome for the comparison of treatment A versus B. Three decision-making zones can be identified, bounded by the thresholds for clinical importance (minimal important difference – MID) for benefit and for harm. The MID for harm for a positive outcome means the threshold at which drug A is less effective than drug B by an amount that is clinically important to patients (favours B).

Figure 2: Illustration of precise and imprecise outcomes based on the confidence interval of outcomes in a forest plot



When the confidence interval of the effect estimate is wholly contained in 1 of the 3 zones (for example, clinically important benefit), we are not uncertain about the size and direction of effect (whether there is a clinically important benefit, or the effect is not clinically important, or there is a clinically important harm), so there is no imprecision.

When a wide confidence interval lies partly in each of 2 zones, it is uncertain in which zone the true value of effect estimate lies, and therefore there is uncertainty over which decision to make (based on this outcome alone). The confidence interval is consistent with 2 decisions and so this is considered to be imprecise in the GRADE analysis and the evidence is downgraded by 1 level ('serious imprecision').

If the confidence interval of the effect estimate crosses into 3 zones, this is considered to be very imprecise evidence because the confidence interval is consistent with 3 clinical decisions and there is a considerable lack of confidence in the results. The evidence is therefore downgraded by 2 levels in the GRADE analysis ('very serious imprecision').

Implicitly, assessing whether the confidence interval is in, or partially in, a clinically important zone, requires the GDG to estimate an MID or to say whether they would make different decisions for the 2 confidence limits.

The literature was searched for established MIDs for the selected outcomes in the evidence reviews but none were found. The GDG were asked whether they were aware of any acceptable MIDs in the clinical community but there were none known. Therefore, the GDG agreed that default values stated in GRADEpro were appropriate for the outcomes. The default thresholds suggested by GRADE are a relative risk reduction of 25% (relative risk of 0.75 for negative outcomes) or a relative risk increase of 25% (risk ration 1.25 for positive outcomes) for dichotomous outcomes. For continuous outcomes, the default approach of multiplying 0.5 by the standard deviation (taken as the median of the standard deviations across the meta-analysed studies) was employed.

4.4.10 Assessing clinical importance

The GDG assessed the evidence by outcome in order to determine if there was, or potentially was, a clinically important benefit, a clinically important harm or no clinically important difference between interventions. To facilitate this, binary outcomes were converted into absolute risk differences (ARDs) using GRADEpro software: the median control group risk across studies was used to calculate the ARD and its 95% CI from the pooled risk ratio.

The assessment of benefit, harm, or no benefit or harm was based on the point estimate of absolute effect for intervention studies in relation to the comparison (or control) event rate.

This assessment was carried out by the GDG for each critical outcome, and an evidence summary table was produced to compile the GDG's assessments of clinical importance per outcome, alongside the evidence quality and the uncertainty in the effect estimate (imprecision).

4.4.11 Evidence statements

Evidence statements are summary statements that are presented after the GRADE profiles, summarising the key features of the clinical effectiveness evidence presented. The wording of the evidence statements reflects the certainty or uncertainty in the estimate of effect. The evidence statements are presented by outcome and encompass the following key features of the evidence:

- the number of studies and the number of participants for a particular outcome
- a brief description of the participants
- an indication of the direction of effect (if one treatment is beneficial or harmful compared to the other, or whether there is no difference between the 2 tested treatments)
- a description of the overall quality of evidence (GRADE overall quality).

4.5 Evidence of cost effectiveness

The GDG is required to make decisions based on the best available evidence of both clinical and cost effectiveness. Guideline recommendations should be based on the expected costs of the different options in relation to their expected health benefits (that is, their 'cost effectiveness') rather than the total implementation cost.[44] Thus, if the evidence suggests that a strategy provides significant health benefits at an acceptable cost per patient treated, it should be recommended even if it would be expensive to implement across the whole population.

Evidence on cost effectiveness related to the key clinical issues being addressed in the guideline was sought. The health economist:

- Undertook a systematic review of the published economic literature.
- Undertook original health economic analyses where appropriate.

4.5.1 Literature review

The health economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts. Full papers were then obtained.
- Reviewed full papers against pre-specified inclusion and exclusion criteria to identify relevant studies (see below for details).
- Critically appraised relevant studies using the economic evaluations checklist as specified in The guidelines manual.[44]
- Extracted key information about the studies' methods and results into evidence tables (included in Appendix H).
- Generated summaries of the evidence in NICE economic evidence profiles (included in the relevant chapter for each review question) – see below for details.

4.5.1.1 Inclusion and exclusion criteria

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost–utility, cost-effectiveness, cost–benefit and cost–consequence analyses) and comparative costing studies that addressed the review question in the relevant population were considered potentially includable as economic evidence.

Studies that only reported cost per hospital (not per patient), or only reported average cost effectiveness without disaggregated costs and effects, were excluded. Literature reviews, abstracts, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

Remaining studies were prioritised for inclusion based on their relative applicability to the development of this guideline and the study limitations. For example, if a high quality, directly applicable UK analysis was available, then other less relevant studies may not have been included. Where exclusions occurred on this basis, this is noted in the relevant section.

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist (Appendix F of The guidelines manual[44] and the health economics review protocol in Appendix C).

When no relevant economic studies were found from the economic literature review, relevant UK NHS unit costs related to the compared interventions were presented to the GDG to inform the possible economic implications of the recommendations.

4.5.1.2 NICE economic evidence profiles

The NICE economic evidence profile has been used to summarise cost and cost-effectiveness estimates. The economic evidence profile shows an assessment of applicability and methodological quality for each economic evaluation, with footnotes indicating the reasons for the assessment. These assessments were made by the health economist using the economic evaluation checklist from The guidelines manual.[44] It also shows the incremental costs, incremental effects (for example, quality-adjusted life years [QALYs]) and incremental cost-effectiveness ratio for the base case

analysis in the evaluation, as well as information about the assessment of uncertainty in the analysis. See Table 6 for more details.

If a non-UK study was included in the profile, the results were converted into pounds sterling using the appropriate purchasing power parity.[47]

Table 6: Content of NICE economic evidence profile

Item	Description
Study	First author name, reference, date of study publication and country perspective.
Applicability	An assessment of applicability of the study to the clinical guideline, the current NHS situation and NICE decision-making[(a)]: • Directly applicable – the study meets all applicability criteria, or fails to meet one or more applicability criteria but this is unlikely to change the conclusions about cost effectiveness. • Partially applicable – the study fails to meet one or more applicability criteria, and this could change the conclusions about cost effectiveness. • Not applicable – the study fails to meet one or more of the applicability criteria, and this is likely to change the conclusions about cost effectiveness. Such studies would usually be excluded from the review.
Limitations	An assessment of methodological quality of the study[(a)]: • Minor limitations – the study meets all quality criteria, or fails to meet one or more quality criteria, but this is unlikely to change the conclusions about cost effectiveness. • Potentially serious limitations – the study fails to meet one or more quality criteria, and this could change the conclusions about cost effectiveness. • Very serious limitations – the study fails to meet one or more quality criteria, and this is highly likely to change the conclusions about cost effectiveness. Such studies would usually be excluded from the review.
Other comments	Particular issues that should be considered when interpreting the study.
Incremental cost	The mean cost associated with one strategy minus the mean cost of a comparator strategy.
Incremental effects	The mean QALYs (or other selected measure of health outcome) associated with one strategy minus the mean QALYs of a comparator strategy.
Cost effectiveness	Incremental cost-effectiveness ratio (ICER): the incremental cost divided by the incremental effects.
Uncertainty	A summary of the extent of uncertainty about the ICER reflecting the results of deterministic or probabilistic sensitivity analyses, or stochastic analyses of trial data, as appropriate.

(a) Applicability and limitations were assessed using the economic evaluation checklist in Appendix G of The guidelines manual (2012)[44]

4.5.2 Undertaking new health economic analysis

As well as reviewing the published economic literature for each review question, as described above, new economic analysis was considered by the health economist in selected areas. Priority areas for new health economic analysis were discussed with the GDG after formation of the review questions and consideration of the available health economic evidence. It was agreed by the GDG that for the review question concerning bariatric surgery for early onset type-2 diabetes the cost-effectiveness evidence that existed was sufficient to base recommendations on. For very-low-calorie diets and follow-up care after surgery the GDG agreed that the long-run data needed to populate a model does not exist. Therefore as the results on any model would be largely driven by assumptions rather than clinical evidence no original economic analysis was conducted. To fully consider cost effectiveness,

quality of life studies were incorporated into threshold analysis to see how effective interventions would need to be to be considered cost effective.

4.5.3 Cost-effectiveness criteria

NICE's report 'Social value judgements: principles for the development of NICE guidance' sets out the principles that GDGs should consider when judging whether an intervention offers good value for money.[43] In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- the intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- the intervention cost less than £20,000 per QALY gained compared with the next best strategy.

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'Recommendations and link to evidence' section of the relevant chapter, with reference to issues regarding the plausibility of the estimate or to the factors set out in 'Social value judgements: principles for the development of NICE guidance'.[43]

If a study reported the cost per life year gained but not QALYs, the cost per QALY gained was estimated by multiplying by an appropriate utility estimate to aid interpretation. The estimated cost per QALY gained is reported in the economic evidence profile with a footnote detailing the life-years gained and the utility value used. When QALYs or life years gained are not used in the analysis, results are difficult to interpret unless one strategy dominates the others with respect to every relevant health outcome and cost.

4.5.4 In the absence of economic evidence

When no relevant published studies were found, and a new analysis was not prioritised, the GDG made a qualitative judgement about cost effectiveness by considering expected differences in resource use between options and relevant UK NHS unit costs, alongside the results of the clinical review of effectiveness evidence.

4.6 Developing recommendations

Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendices G and H. Excluded evidence can be found in Appendices J and K.
- Summary of clinical and economic evidence and quality (as presented in Chapters 6-8).
- Forest plots (Appendix I).

Recommendations were drafted on the basis of the GDG interpretation of the available evidence, taking into account the balance of benefits, harms and costs between different courses of action. Firstly, the net benefit over harm (clinical effectiveness) was considered, focusing on the critical outcomes. When this was done informally, the GDG took into account the clinical benefits and harms when one intervention was compared with another. The assessment of net benefit was moderated by the importance placed on the outcomes (the GDG's values and preferences), and the confidence the GDG had in the evidence (evidence quality). Secondly, it was assessed whether the net benefit justified any differences in costs.

When clinical and economic evidence was of poor-quality, conflicting, or absent, the GDG drafted recommendations based on their expert opinion. The considerations for making consensus-based

recommendations include the balance between potential harms and benefits, the economic costs compared to the economic benefits, current practices, and recommendations made in other relevant guidelines, patient preferences and equality issues. The GDG also considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation (see Section 6.6.1 below).

The wording of recommendations was agreed by the GDG and focused on the following factors:

- The actions health professionals need to take.
- The information readers need to know.
- The strength of the recommendation (for example the word 'offer' was used for strong recommendations and 'consider' for weak recommendations).
- The involvement of patients (and their carers if needed) in decisions on treatment and care.
- Consistency with NICE's standard advice on recommendations about drugs, waiting times and ineffective interventions.

The main considerations specific to each recommendation are outlined in the 'Recommendations and link to evidence' sections within each chapter.

4.6.1 Research recommendations

When areas were identified for which good evidence was lacking, the GDG considered making recommendations for future research. Decisions about inclusion were based on factors such as:

- the importance to patients or the population
- national priorities
- potential impact on the NHS and future NICE guidance
- ethical and technical feasibility.

4.6.2 Validation process

This guidance is subject to a 4-week public consultation and feedback as part of the quality assurance and peer review of the document. All comments received from registered stakeholders are responded to in turn and posted on the NICE website after publication of the guideline.

4.6.3 Updating the guideline

A formal review of the need to update a guideline is usually undertaken by NICE after its publication. NICE will conduct a review to determine whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an update.

4.6.4 Disclaimer

Health care providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by practitioners in light of individual patient circumstances, the wishes of the patient, clinical expertise and resources.

The National Clinical Guideline Centre disclaims any responsibility for damages arising out of the use or non-use of this guideline and the literature used in support of this guideline.

4.6.5 Funding

The National Clinical Guideline Centre was commissioned by the National Institute for Health and Care Excellence to undertake the work on this guideline.

5 Guideline summary

5.1 Algorithm

Figure 3: Very- low- calorie diets (VLCD)

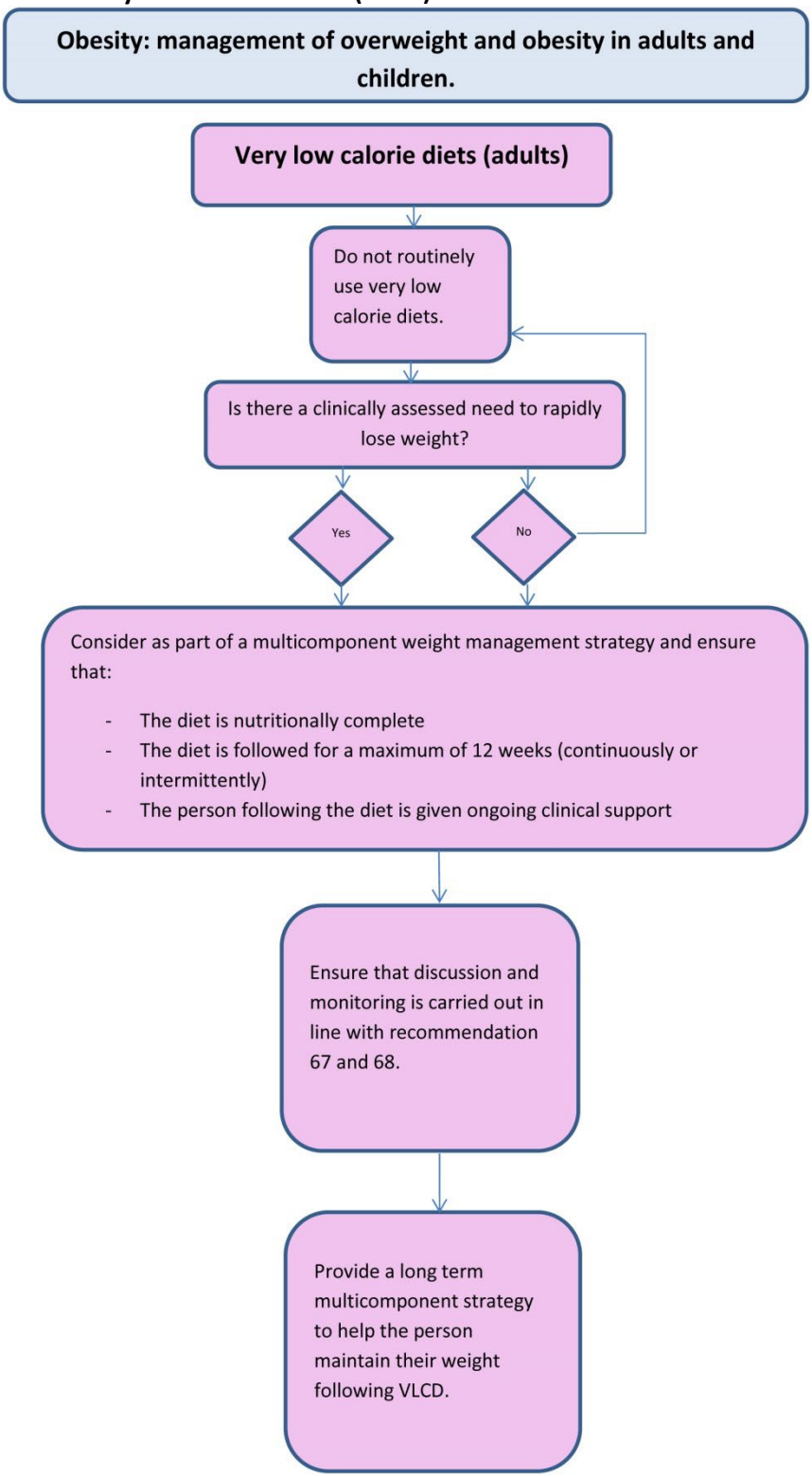


Figure 4: Bariatric surgery in people with type 2 diabetes

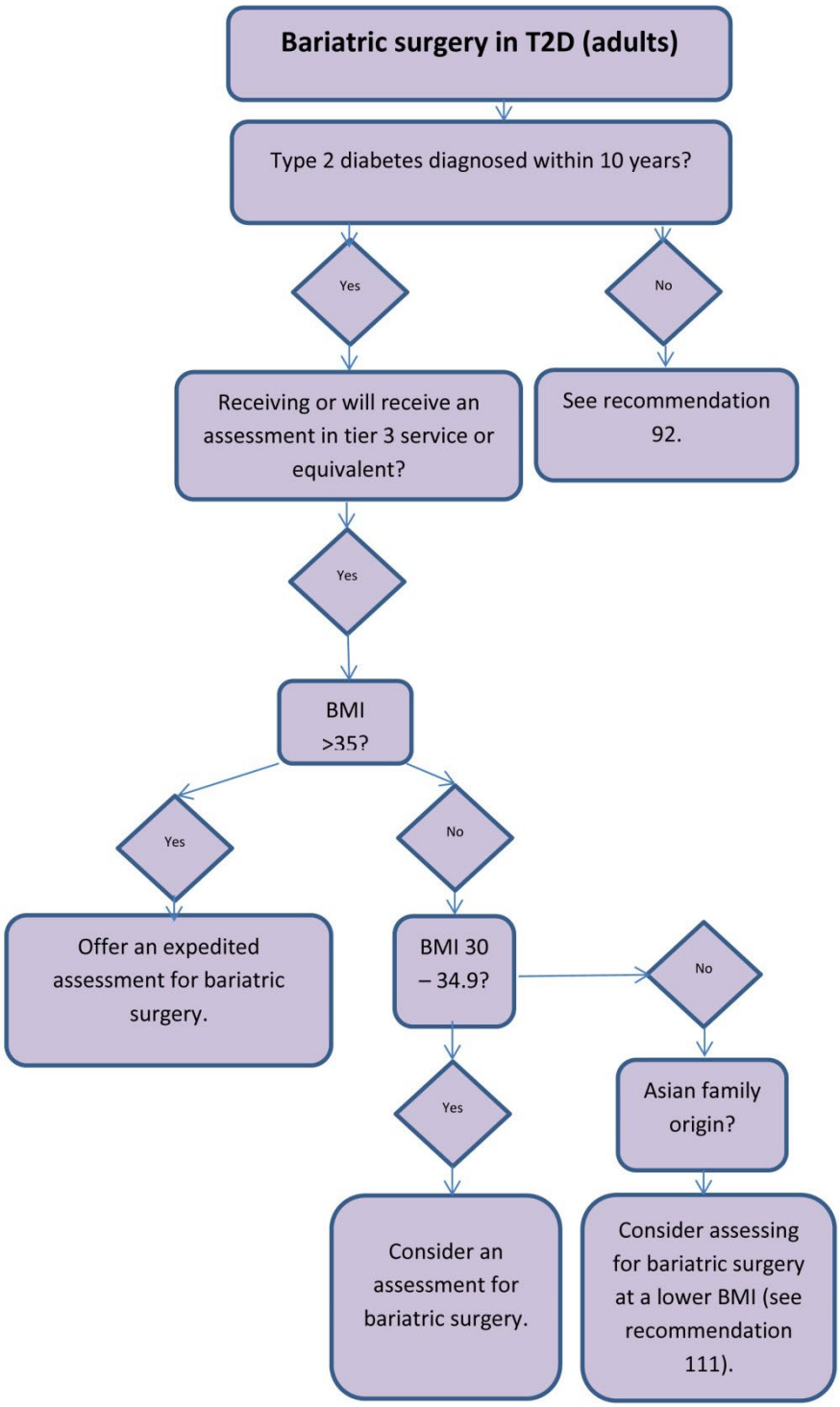


Figure 5: Follow-up care packages after bariatric surgery

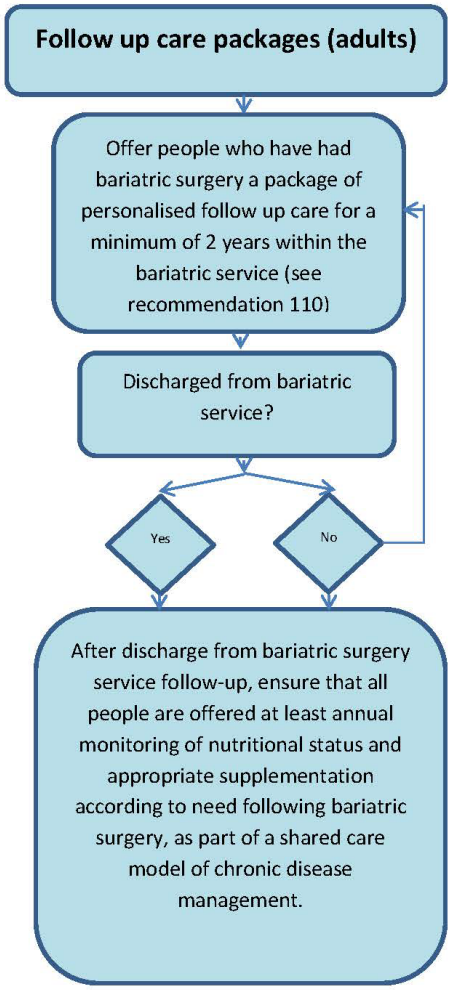
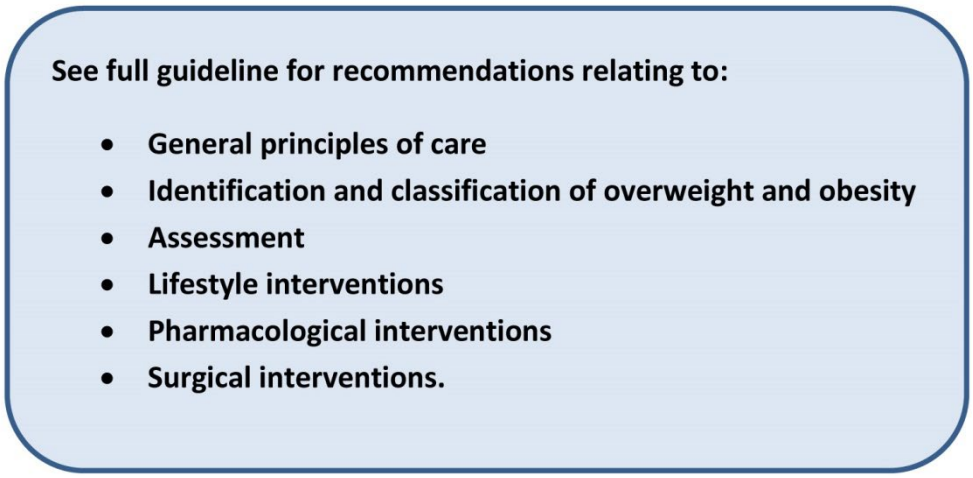


Figure 6: 2006 recommendations



6 Full list of recommendations

6.1 Generic principles of care

6.1.1 Adults

1. Equip specialist settings for treating people who are severely obese with, for example, special seating and adequate weighing and monitoring equipment. Ensure hospitals have access to specialist equipment – such as larger scanners and beds –when providing general care for people who are severely obese. [2006, amended 2014]

2. Discuss the choice of interventions for weight management with the person. The choice of intervention should be agreed with the person. [2006, amended 2014]

3. Tailor the components of the planned weight management programme to the person's preferences, initial fitness, health status and lifestyle. [2006]

6.1.2 Children

4. Coordinate the care of children and young people around their individual and family needs. Comply with the approaches outlined in the Department of Health's A call to action on obesity in England[a].[2006, amended 2014]

5. Aim to create a supportive environment[b] that helps a child who is overweight or who has obesity, and their family, make lifestyle changes. [2006, amended 2014]

6. Make decisions about the care of a child who is overweight or has obesity (including assessment and agreeing goals and actions) together with the child and family. Tailor interventions to the needs and preferences of the child and the family. [2006]

7. Ensure that interventions for children who are overweight or have obesity address lifestyle within the family and in social settings. [2006, amended 2014]

8. Encourage parents (or carers) to take main responsibility for lifestyle changes in children who are overweight or obese, especially if they are younger than 12 years. Take into account the age and maturity of the child, and the preferences of the child and the parents. [2006]

6.1.3 Adults and children

9. Offer regular, non-discriminatory long-term follow-up by a trained professional. Ensure continuity of care in the multidisciplinary team through good record keeping. [2006]

6.2 Identification and classification of overweight and obesity

10. Use clinical judgement to decide when to measure a person's height and weight. Opportunities include registration with a general practice, consultation for related conditions (such as type 2 diabetes and cardiovascular disease) and other routine health checks. [2006]

[a] Recommendations on the management of overweight and obesity in children and young people can be found in Managing overweight and obesity among children and young people: lifestyle weight management services (NICE guideline 47).
[b] The GDG noted that 'environment' could include settings other than the home, for example, schools.

6.3 Measures of overweight and obesity

11. Use BMI as a practical estimate of adiposity in adults. Interpret BMI with caution because it is not a direct measure of adiposity. [2006, amended 2014]

12. Think about using waist circumference, in addition to BMI, in people with a BMI less than 35 kg/m^2.[c] [2006, amended 2014]

6.3.1 Children

13. Use BMI (adjusted for age and gender[d]) as a practical estimate of adiposity in children and young people. Interpret BMI with caution because it is not a direct measure of adiposity. [2006, amended 2014]

14. Waist circumference is not recommended as a routine measure. Use it to give additional information on the risk of developing other long-term health problems. [2006, amended 2014]

6.3.2 Adults and children

15. Do not use bioimpedance as a substitute for BMI as a measure of general adiposity. [2006, amended 2014]

6.4 Classification of overweight and obesity

6.4.1 Adults

16. Define the degree of overweight or obesity in adults using the following table:

Classification	BMI (kg/m^2)
Healthy weight	18.5–24.9
Overweight	25–29.9
Obesity I	30–34.9
Obesity II	35–39.9
Obesity III	40 or more

17. Interpret BMI with caution in highly muscular adults because it may be a less accurate measure of adiposity in this group. Some other population groups, such as people of Asian family origin and older people, have comorbidity risk factors that are of concern at different BMIs (lower for adults of an Asian family origin and higher for older people[e]). Use clinical judgement when considering risk factors in these groups, even in people not classified as overweight or obese, using the classification in recommendation 15. [2006]

18. Base assessment of the health risks associated with being overweight or obese in adults on BMI and waist circumference as follows:

[c] Further information on the use of BMI and waist circumference can be found in BMI and waist circumference – black, Asian and minority ethnic groups (NICE guideline 46).

[d] Where available, BMI z-scores or the Royal College of Paediatrics and Child Health UK-WHO growth charts may be used to calculate BMI in children and young people. The childhood and puberty close monitoring (CPCM) form may be used for longitudinal BMI monitoring in children over 4.

[e] Further information on the use of BMI and waist circumference can be found in BMI and waist circumference – black, Asian and minority ethnic groups (NICE guideline 46).

BMI classification	Waist circumference		
	Low	High	Very high
Overweight	No increased risk	Increased risk	High risk
Obesity I	Increased risk	High risk	Very high risk
For men, waist circumference of less than 94 cm is low, 94–102 cm is high and more than 102 cm is very high For women, waist circumference of less than 80 cm is low, 80–88 cm is high and more than 88 cm is very high			

[2006]

19. Give adults information about their classification of clinical obesity and the impact this has on risk factors for developing other long-term health problems. [2006]

20. Base the level of intervention to discuss with the patient initially as follows:

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

The level of intervention should be higher for patients with comorbidities (see section 5.5 for details), regardless of their waist circumference. Adjust the approach as needed, depending on the person's clinical need and potential to benefit from losing weight. [2006]

6.4.2 Children

21. Relate BMI measurement in children and young people to the UK 1990 BMI charts[f]. to give age- and gender-specific information [2006, amended 2014]

22. Tailored clinical intervention should be considered for children with a BMI at or above the 91st centile, depending on the needs of the individual child and family. [2006]

[f] Where available, BMI z scores or the Royal College of Paediatrics and Child Health UK-WHO growth charts may be used to calculate BMI in children and young people. The childhood and puberty close monitoring (CPCM) form may be used for longitudinal BMI monitoring in children over 4.

6.5 Assessment

6.5.1 Adults and children

23. Make an initial assessment (see recommendations 28 and 30), then use clinical judgement to investigate comorbidities and other factors to an appropriate level of detail, depending on the person, the timing of the assessment, the degree of overweight or obesity, and the results of previous assessments. [2006]

24. Manage comorbidities when they are identified; do not wait until the person has lost weight. [2006]

25. Offer people who are not yet ready to change the chance to return for further consultations when they are ready to discuss their weight again and willing or able to make lifestyle changes. Give them information on the benefits of losing weight, healthy eating and increased physical activity.[2006]

26. Recognise that surprise, anger, denial or disbelief about their health situation may diminish people's ability or willingness to change. Stress that obesity is a clinical term with specific health implications, rather than a question of how people look; this may reduce any negative feelings.

    During the consultation:

- Assess the person's view of their weight and the diagnosis, and possible reasons for weight gain.
- Explore eating patterns and physical activity levels.
- Explore any beliefs about eating, physical activity and weight gain that are unhelpful if the person wants to lose weight.
- Be aware that people from certain ethnic and socioeconomic backgrounds may be at greater risk of obesity, and may have different beliefs about what is a healthy weight and different attitudes towards weight management.
- Find out what the person has already tried and how successful this has been, and what they learned from the experience.
- Assess the person's readiness to adopt changes.
- Assess the person's confidence in making changes. [2006, amended 2014]

27. Give people and their families and/or carers information on the reasons for tests, how the tests are done and their results and meaning. If necessary, offer another consultation to fully explore the options for treatment or discuss test results. [2006, amended 2014]

6.5.2 Adults

28. Take measurements (see recommendations in section 5.2) to determine degree of overweight or obesity and discuss the implications of the person's weight. Then, assess:

- any presenting symptoms
- any underlying causes of being overweight or obese
- eating behaviours
- any comorbidities (for example type 2 diabetes, hypertension, cardiovascular disease, osteoarthritis, dyslipidaemia and sleep apnoea)

- any risk factors assessed using lipid profile (preferably done when fasting), blood pressure measurement and HbA_{1c} measurement
- the person's lifestyle (diet and physical activity)
- any psychosocial distress
- any environmental, social and family factors, including family history of overweight and obesity and comorbidities
- the person's willingness and motivation to change lifestyle
- the potential of weight loss to improve health
- any psychological problems[g]
- any medical problems and medication
- the role of family and care workers in supporting people with learning disabilities to make lifestyle changes. [2006, amended 2014]

29. Consider referral to tier 3 services[h] if:

- the underlying causes of being overweight or obese need to be assessed
- the person has complex disease states or needs that cannot be managed adequately in tier 2 (for example, the additional support needs of people with learning disabilities)
- conventional treatment has been unsuccessful
- drug treatment is being considered for a person with a BMI of more than 50 kg/m^2
- specialist interventions (such as a very-low-calorie diet) may be needed
- surgery is being considered. [2006, amended 2014]

6.5.3 Children

30. Assessment of comorbidity should be considered for children with a BMI at or above the 98th centile. [2006]

31. Take measurements to determine degree of overweight or obesity and raise the issue of weight with the child and family, then assess:

- presenting symptoms and underlying causes of being overweight or obese
- willingness and motivation to change
- comorbidities (such as hypertension, hyperinsulinaemia, dyslipidaemia, type 2 diabetes, psychosocial dysfunction and exacerbation of conditions such as asthma)
- any risk factors assessed using lipid profile (preferably done when fasting), blood pressure measurement and HbA_{1c} measurement
- psychosocial distress, such as low self-esteem, teasing and bullying[i]
- family history of being overweight or obese and comorbidities
- the child and family's willingness and motivation to change lifestyle
- lifestyle (diet and physical activity)
- environmental, social and family factors that may contribute to being overweight or obese, and the success of treatment

[g] Further recommendations can be found in Managing overweight and obesity among children and young people: lifestyle weight management services (NICE guideline PH47).
[h] For more information on tier 3 services, see NHS England's report on Joined up clinical pathways for obesity.
[i] Further recommendations can be found in Managing overweight and obesity among children and young people: lifestyle weight management services (NICE guideline PH47).

- growth and pubertal status
- any medical problems and medication
- the role of family and care workers in supporting people with learning disabilities to make lifestyle changes. [2006, amended 2014]

32. Consider referral to an appropriate specialist for children who are overweight or obese and have significant comorbidities or complex needs (for example, learning disabilities or other additional support needs). [2006, amended 2014]

33. In tier 3 services, assess associated comorbidities and possible causes for children and young people who are overweight or who have obesity. Use investigations such as:

- blood pressure measurement
- lipid profile, preferably while fasting
- fasting insulin
- fasting glucose levels and oral glucose tolerance test
- liver function
- endocrine function.

Interpret the results of any tests used in the context of how overweight or obese the child is, the child's age, history of comorbidities, possible genetic causes and any family history of metabolic disease related to being overweight or obese. [2006, amended 2014]

34. Make arrangements for transitional care for children and young people who are moving from paediatric to adult services. [2006]

6.6 Lifestyle interventions

6.6.1 Adults and children

35. Multicomponent interventions are the treatment of choice. Ensure weight management programmes include behaviour change strategies (see recommendations 48-50) to increase people's physical activity levels or decrease inactivity, improve eating behaviour and the quality of the person's diet, and reduce energy intake. [2006, amended 2014]

36. When choosing treatments, take into account:

- the person's individual preference and social circumstance and the experience and outcome of previous treatments (including whether there were any barriers)
- the person's level of risk, based on BMI and, where appropriate, waist circumference (see recommendations 18-20)
- any comorbidities. [2006, amended 2014]

37. Document the results of any discussion. Keep a copy of the agreed goals and actions (ensure the person also does this), or put this in the person's notes.[2006, amended 2014]

38. Offer support depending on the person's needs, and be responsive to changes over time. [2006]

39. Ensure any healthcare professionals who deliver interventions for weight management have relevant competencies and have had specific training. [2006, amended 2014]

40. Provide information in formats and languages that are suited to the person. Use everyday, jargon-free language and explain any technical terms when talking to the person and their family or carers. Take into account the person's:

- age and stage of life
- gender
- cultural needs and sensitivities
- ethnicity
- social and economic circumstances
- specific communication needs (for example because of learning disabilities, physical disabilities or cognitive impairments due to neurological conditions). [2006, amended 2014]

41. Praise successes – however small – at every opportunity to encourage the person through the difficult process of changing established behaviour. [2006]

42. Give people who are overweight or obese, and their families and/or carers, relevant information on:

- being overweight and obesity in general, including related health risks
- realistic targets for weight loss; for adults, please see NICE's guideline on managing overweight and obesity in adults
- the distinction between losing weight and maintaining weight loss, and the importance of developing skills for both; advise them that the change from losing weight to maintenance typically happens after 6-9 months of treatment
- realistic targets for outcomes other than weight loss, such as increased physical activity and healthier eating
- diagnosis and treatment options
- healthy eating in general[j]
- medication and side effects
- surgical treatments
- self-care
- voluntary organisations and support groups and how to contact them.

Ensure there is adequate time in the consultation to provide information and answer questions. [2006, amended 2014]

43. If a person (or their family or carers) does not feel this is the right time for them to take action, explain that advice and support will be available in the future whenever they need it. Provide contact details so that the person can get in touch when they are ready. [2006, amended 2014]

6.6.2 Adults

44. Encourage the person's partner or spouse to support any weight management programme.[2006]

[j] Further information on healthy eating can be found on NHS Choices.

45. Base the level of intensity of the intervention on the level of risk and the potential to gain health benefits (see recommendation 20). [2006]

6.6.3 Children

46. Be aware that the aim of weight management programmes for children and young people can vary. The focus may be on either weight maintenance or weight loss, depending on the person's age and stage of growth. [2006, amended 2014]

47. Encourage parents of children and young people who are overweight or obese to lose weight if they are also overweight or obese. [2006]

6.7 Behavioural interventions

6.7.1 Adults and children

48. Deliver any behavioural intervention with the support of an appropriately trained professional. [2006]

6.7.2 Adults

49. Include the following strategies in behavioural interventions for adults, as appropriate:

- o self-monitoring of behaviour and progress
- o stimulus control
- o goal setting
- o slowing rate of eating
- o ensuring social support
- o problem solving
- o assertiveness
- o cognitive restructuring (modifying thoughts)
- o reinforcement of changes
- o relapse prevention
- o strategies for dealing with weight regain. [2006]

6.7.3 Children

50. Include the following strategies in behavioural interventions for children, as appropriate:

- o stimulus control
- o self-monitoring
- o goal setting
- o rewards for reaching goals
- o problem solving.

Give praise to successes and encourage parents to role-model desired behaviours. [2006, amended 2014]

6.8 Physical activity

6.8.1 Adults

51. Encourage adults to increase their level of physical activity even if they do not lose weight as a result, because of the other health benefits it can bring (for example, reduced risk of type 2 diabetes and cardiovascular disease). Encourage adults to do at least 30 minutes of moderate or greater intensity physical activity on 5 or more days a week. The activity can be in 1 session or several sessions lasting 10 minutes or more.[2006]

52. Advise that to prevent obesity, most people may need to do 45–60 minutes of moderate-intensity activity a day, particularly if they do not reduce their energy intake. Advise people who have been obese and have lost weight that they may need to do 60–90 minutes of activity a day to avoid regaining weight.[2006]

53. Encourage adults to build up to the recommended activity levels for weight maintenance, using a managed approach with agreed goals.

Recommend types of physical activity, including:

- activities that can be incorporated into everyday life, such as brisk walking, gardening or cycling[k]
- supervised exercise programmes
- other activities, such as swimming, aiming to walk a certain number of steps each day, or stair climbing.

Take into account the person's current physical fitness and ability for all activities. Encourage people to also reduce the amount of time they spend inactive, such as watching television, using a computer or playing video games. [2006]

6.8.2 Children

54. Encourage children and young people to increase their level of physical activity, even if they do not lose weight as a result, because of the other health benefits exercise can bring (for example, reduced risk of type 2 diabetes and cardiovascular disease). Encourage children to do at least 60 minutes of moderate or greater intensity physical activity each day. The activity can be in 1 session or several sessions lasting 10 minutes or more. [2006]

55. Be aware that children who are already overweight may need to do more than 60 minutes' activity.[2006, amended 2014]

56. Encourage children to reduce inactive behaviours, such as sitting and watching television, using a computer or playing video games. [2006]

57. Give children the opportunity and support to do more exercise in their daily lives (for example, walking, cycling, using the stairs and active play[l]). Make the choice of activity with the child, and ensure it is appropriate to the child's ability and confidence. [2006]

[k] Further recommendations can be found in Walking and cycling: local measures to promote walking and cycling as forms of travel or recreation (NICE guideline PH41).

[l] Further recommendations can be found in Walking and cycling: local measures to promote walking and cycling as forms of travel or recreation (NICE guideline PH41).

58. Give children the opportunity and support to do more regular, structured physical activity, (for example football, swimming or dancing). Make the choice of activity with the child, and ensure it is appropriate to the child's ability and confidence. [2006]

6.9 Dietary

6.9.1 Adults and children

59. Tailor dietary changes to food preferences and allow for a flexible and individual approach to reducing calorie intake. [2006]

60. Do not use unduly restrictive and nutritionally unbalanced diets, because they are ineffective in the long term and can be harmful. [2006, amended 2014]

61. Encourage people to improve their diet even if they do not lose weight, because there can be other health benefits. [2006]

6.9.2 Adults

62. The main requirement of a dietary approach to weight loss is that total energy intake should be less than energy expenditure. [2006]

63. Diets that have a 600 kcal/day deficit (that is, they contain 600 kcal less than the person needs to stay the same weight) or that reduce calories by lowering the fat content (low-fat diets), in combination with expert support and intensive follow-up, are recommended for sustainable weight loss. [2006]

64. Consider low-calorie diets (800–1600 kcal/day), but be aware these are less likely to be nutritionally complete. [2006, amended 2014]

65. Do not routinely use very-low- calorie diets (800 kcal/day or less) to manage obesity (defined as BMI over 30). [new 2014]

66. Only consider very-low-calorie diets, as part of a multicomponent weight management strategy, for people who are obese and who have a clinically-assessed need to rapidly lose weight (for example, people who need joint replacement surgery or who are seeking fertility services). Ensure that:

- the diet is nutritionally complete
- the diet is followed for a maximum of 12 weeks (continuously or intermittently)
- the person following the diet is given ongoing clinical support. [new 2014]

67. Before starting someone on a very-low-calorie diet as part of a multicomponent weight management strategy:

- Consider counselling and assess for eating disorders or other psychopathology to make sure the diet is appropriate for them
- Discuss the risks and benefits with them

- Tell them that this is not a long-term weight management strategy, and that regaining weight may happen and is not because of their own or their clinician's failure
- Discuss the reintroduction of food following a liquid diet with them. [new 2014]

68. Provide a long-term multicomponent strategy to help the person maintain their weight after the use of a very-low-calorie diet. (See recommendation 35). [new 2014]

69. Encourage people to eat a balanced diet in the long term, consistent with other healthy eating advice[m]. [2006, amended 2014]

6.9.3 Children

70. A dietary approach alone is not recommended. It is essential that any dietary recommendations are part of a multicomponent intervention.[2006]

71. Any dietary changes should be age appropriate and consistent with healthy eating advice.[2006]

72. For overweight and obese children and young people, total energy intake should be below their energy expenditure. Changes should be sustainable.[2006, amended 2014]

6.10 Pharmacological interventions

6.10.1 Adults

73. Consider pharmacological treatment only after dietary, exercise and behavioural approaches have been started and evaluated.[2006]

74. Consider drug treatment for people who have not reached their target weight loss or have reached a plateau on dietary, activity and behavioural changes.[2006]

75. Make the decision to start drug treatments after discussing the potential benefits and limitations with the person, including the mode of action, adverse effects and monitoring requirements, and the potential impact on the person's motivation. Make arrangements for appropriate healthcare professionals to offer information, support and counselling on additional diet, physical activity and behavioural strategies when drug treatment is prescribed. Provide information on patient support programmes. [2006, amended 2014]

6.10.2 Children

76. Drug treatment is not generally recommended for children younger than 12 years. [2006]

77. In children younger than 12 years, drug treatment may be used only in exceptional circumstances, if severe comorbidities are present. Prescribing should be started and monitored only in specialist paediatric settings.[2006, amended 2014]

78. In children aged 12 years and older, treatment with orlistat[n] is recommended only if physical comorbidities (such as orthopaedic problems or sleep apnoea) or severe psychological

[m] Further information on healthy eating can be found on NHS Choices .

[n] At the time of publication (October 2014), orlistat did not have a UK marketing authorisation for use in children for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision.

comorbidities are present. Treatment should be started in a specialist paediatric setting, by multidisciplinary teams with experience of prescribing in this age group. [2006, amended 2014]

79. Do not give orlistat to children for obesity unless prescribed by a multidisciplinary team with expertise in:

- drug monitoring
- psychological support
- behavioural interventions
- interventions to increase physical activity
- interventions to improve diet. [2006, amended 2014]

80. Drug treatment may be continued in primary care for example with a shared care protocol if local circumstances and/or licensing allow. [2006, amended 2014]

6.11 Continued prescribing and withdrawal

6.11.1 Adults and children

81. Pharmacological treatment may be used to maintain weight loss rather than to continue to lose weight.[2006]

82. If there is concern about micronutrient intake adequacy, a supplement providing the reference nutrient intake for all vitamins and minerals should be considered, particularly for vulnerable groups such as older people (who may be at risk of malnutrition) and young people (who need vitamins and minerals for growth and development). [2006]

83. Offer support to help maintain weight loss to people whose drug treatment is being withdrawn; if they did not reach their target weight, their self-confidence and belief in their ability to make changes may be low. [2006]

6.11.2 Adults

84. Monitor the effect of drug treatment and reinforce lifestyle advice and adherence through regular review. [2006, amended 2014]

85. Consider withdrawing drug treatment in people who have not reached weight loss targets (see recommendation 88 for details). [2006]

86. Rates of weight loss may be slower in people with type 2 diabetes, so less strict goals than those for people without diabetes may be appropriate. Agree the goals with the person and review them regularly. [2006]

87. Only prescribe orlistat as part of an overall plan for managing obesity in adults who meet 1 of the following criteria:

- a BMI of 28 kg/m^2 or more with associated risk factors
- a BMI of 30 kg/m^2 or more. [2006]

Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

88. Continue orlistat therapy beyond 3 months only if the person has lost at least 5% of their initial body weight since starting drug treatment. (See also recommendation 86 for advice on targets for people with type 2 diabetes).[2006]

89. Make the decision to use drug treatment for longer than 12 months (usually for weight maintenance) after discussing potential benefits and limitations with the person. [2006]

90. The co-prescribing of orlistat with other drugs aimed at weight reduction is not recommended. [2006]

6.11.3 Children

91. If orlistat[o] is prescribed for children, a 6-12 month trial is recommended, with regular review to assess effectiveness, adverse effects and adherence. [2006, amended 2014]

6.12 Surgical interventions

92. 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 other significant disease (for example, type 2 diabetes or high blood pressure) that could be improved if they lost weight.
- All appropriate non-surgical measures have been tried but 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[p].
- The person is generally fit for anaesthesia and surgery.
- The person commits to the need for long-term follow-up.

See recommendations 103 and 104 for additional criteria to use when assessing children, and recommendation 98 for additional criteria for adults. See also recommendations 109–111 for additional criteria for people with type 2 diabetes [2006, amended 2014]

93. The hospital specialist and/or bariatric surgeon should discuss the following with people who are severely obese if they are considering surgery to aid weight reduction:

- the potential benefits
- the longer-term implications of surgery
- associated risks
- complications
- perioperative mortality.

The discussion should also include the person's family, as appropriate. [2006, amended 2014]

94. Choose the surgical intervention jointly with the person, taking into account:

[o] At the time of publication (October 2014), orlistat did not have a UK marketing authorisation for use in children for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicinesfor further information.

[p] For more information on tier 3 services, see NHS England's report on Joined up clinical pathways for obesity.

- the degree of obesity
- comorbidities
- the best available evidence on effectiveness and long-term effects
- the facilities and equipment available
- the experience of the surgeon who would perform the operation. [2006]

95. Provide regular, specialist postoperative dietetic monitoring, including:

- information on the appropriate diet for the bariatric procedure
- monitoring of the person's micronutrient status
- information on patient support groups
- individualised nutritional supplementation, support and guidance to achieve long-term weight loss and weight maintenance. [2006]

96. Arrange prospective audit so that the outcomes and complications of different procedures, the impact on quality of life and nutritional status, and the effect on comorbidities can be monitored in both the short and the long term[q]. [2006, amended 2014]

97. The surgeon in the multidisciplinary team should:

- have had a relevant supervised training programme
- have specialist experience in bariatric surgery
- submit data for a national clinical audit scheme[r]. [2006, amended 2014]

6.12.1 Adults

98. In addition to the criteria listed in 92, 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. [2006, amended 2014]

99. Orlistat may be used to maintain or reduce weight before surgery for people who have been recommended surgery as a first-line option, if it is considered that the waiting time for surgery is excessive. [2006, amended 2014]

100. Surgery for obesity should be undertaken only by a multidisciplinary team that can provide:

- preoperative assessment, including a risk-benefit analysis that includes preventing complications of obesity, and specialist assessment for eating disorder(s)
- information on the different procedures, including potential weight loss and associated risks
- regular postoperative assessment, including specialist dietetic and surgical follow-up (see 112)
- management of comorbidities
- psychological support before and after surgery
- information on, or access to, plastic surgery (such as apronectomy) when appropriate
- access to suitable equipment, including scales, theatre tables, Zimmer frames, commodes, hoists, bed frames, pressure-relieving mattresses and seating suitable for people undergoing bariatric surgery, and staff trained to use them. [2006]

[q] The National Bariatric Surgery Registry is now available to conduct national audit for a number of agreed outcomes.
[r] The National Bariatric Surgery Registry is now available to conduct national audit for a number of agreed outcomes.

101. Carry out a comprehensive preoperative assessment of any psychological or clinical factors that may affect adherence to postoperative care requirements (such as changes to diet) before performing surgery. [2006, amended 2014]

102. Revisional surgery (if the original operation has failed) should be undertaken only in specialist centres by surgeons with extensive experience because of the high rate of complications and increased mortality. [2006]

6.12.2 Children

103. Surgical intervention is not generally recommended in children or young people.[2006]

104. Bariatric surgery may be considered for young people only in exceptional circumstances, and if they have achieved or nearly achieved physiological maturity. [2006]

105. Surgery for obesity should be undertaken only by a multidisciplinary team that can provide paediatric expertise in:

- preoperative assessment, including a risk-benefit analysis that includes preventing complications of obesity, and specialist assessment for eating disorder(s)
- information on the different procedures, including potential weight loss and associated risks
- regular postoperative assessment, including specialist dietetic and surgical follow-up
- management of comorbidities
- psychological support before and after surgery
- information on or access to plastic surgery (such as apronectomy) when appropriate
- access to suitable equipment, including scales, theatre tables, Zimmer frames, commodes, hoists, bed frames, pressure-relieving mattresses and seating suitable for children and young people undergoing bariatric surgery, and staff trained to use them. [2006]

106. Coordinate surgical care and follow-up around the child or young person and their family's needs. Comply with the approaches outlined in the Department of Health's A call to action on obesity in England. [2006, amended 2014]

107. Ensure all young people have had a comprehensive psychological, educational, family and social assessment before undergoing bariatric surgery .[2006, amended 2014]

108. Perform a full medical evaluation, including genetic screening or assessment before surgery to exclude rare, treatable causes of obesity. [2006]

6.13 Bariatric surgery in people with recent onset type 2 diabetes

109. Offer an expedited assessment for bariatric surgery to people who with a BMI of 35 or over who have recent-onset type 2 diabetes[s] as long as they are also receiving or will receive assessment in a tier 3 service (or equivalent). [new 2014]

110. Consider an assessment for bariatric surgery in people with a BMI of 30-34.9 who have recent-onset type 2 diabetes[t] as long as they are also receiving or will receive assessment in a tier 3 service (or equivalent). [new 2014]

111. Consider an assessment for bariatric surgery in people of Asian family origin who have recent-onset type 2 diabetes[u] at a lower BMI than other populations (see recommendation 17) as long as they are also receiving or will receive assessment in a tier 3 service (or equivalent). [new 2014]

6.14 Follow up care

112. Offer people who have had bariatric surgery a follow-up care package for a minimum of 2 years within the bariatric service. This should include:

- monitoring nutritional intake (including protein and vitamins) and mineral deficiencies
- monitoring for comorbidities
- medication review
- dietary and nutritional assessment, advice and support
- physical activity advice and support
- psychological support tailored to the individual
- information about professionally-led or peer-support groups. [new 2014]

113. After discharge from bariatric surgery service follow-up, ensure that all people are offered at least annual monitoring of nutritional status and appropriate supplementation according to need following bariatric surgery, as part of a shared care model of chronic disease management. [new 2014]

6.15 Key research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

Follow-up care after bariatric surgery

Do post-operative lifestyle intervention programmes (exercise, behavioural or dietary) improve weight loss and weight-loss maintenance following bariatric surgery?

Long-term outcomes of bariatric surgery on people with type 2 diabetes

[s] The GDG considered that recent-onset type 2 diabetes would include those people whose diagnosis has been made within a 10-year time frame.

[t] The GDG considered that recent-onset type 2 diabetes would include those people whose diagnosis has been made within a 10-year time frame.

[u] The GDG considered that recent-onset type 2 diabetes would include those people whose diagnosis has been made within a 10-year time frame.

What is the long-term effect of bariatric surgery on diabetes-related complications and quality of life in people with type 2 diabetes compared with optimal medical treatment?

Bariatric surgery in children and young people

What are the long-term outcomes of bariatric surgery in children and young people with obesity?

Obesity management for people with a condition associated with an increased risk of obesity

What is the best way to deliver obesity management interventions to people with particular conditions associated with increased risk of obesity (such as people with a physical disability that limits mobility, a learning disability or enduring mental health difficulties)?

Long-term effect of very-low-calorie diets on people with a BMI of 40kg/m² or more

What are the long-term effects of using very-low-calorie diets (VLCDs) versus low-calorie diets (LCDs) on weight and quality of life in patients with a BMI of 40 kg/m^2 or more, including the impact on weight cycling?

6.16 How this clinical guideline was updated

Methods used to develop recommendations from CG43, as well as the accompanying text from CG43, can be found in Appendices M and N.

Appendix Q contains details of the amendments to recommendations from the original guideline. All recommendations have been updated to ensure that they comply with the NICE policy on non-discrimination and, where appropriate, have been amended or the wording changed in line with current NICE house style.

Appendix Q also contains details of recommendations which have been deleted from the current guideline and an explanation as to why these recommendations have been removed.

7 Very-low-calorie diets

7.1 Introduction

Obesity is a serious public health issue and the most common interventions are diet and exercise. The use of very-low-calorie diets (VLCDs) is sometimes considered for weight management in the NHS and in commercial programmes. There is a need for long-term comparison with conventional dietary interventions to assess clinical effectiveness. VLCDs are defined as hypocaloric diets which provide between 450 to 800 kcal per day and are relatively enriched in protein of high biological value. They must contain the full complement of vitamins, minerals, electrolytes and fatty acids. They are usually in a liquid formulation and are intended to completely replace other food intake in a weight loss programme for a specific period of time.

NICE CG43 (2006) reviewed and approved the short-term use of VLCDs in treatment of the obese person. The provision of very-low-calorie diets on the NHS is an emerging intervention option, and often used by people with a high BMI, despite a lack of published literature on the use of VLCDs in this group. However, it is noted that a large number of individuals purchase these limited calorie total diet replacements from commercial providers.

CG43 recommended the use of VLCDs in people who are obese and have reached a plateau in weight loss. The care and management of these people is likely to be delivered within specialist services. Moreover, the GDG recognise that attendance at NHS care will vary but that it is likely that people with comorbidity would attend at a GP surgery. It is important to assess whether the provision of VLCDs in this population is of added benefit compared to the usual care provided at this level.

The GDG wished to determine the long-term efficacy of VLCDs as it is currently unknown. The potential increased use of VLCD in the NHS requires evidence of improved patient outcomes without compromising patient safety and quality of care. This includes assessing evidence of reduction in comorbidities with long-term maintenance of weight loss and the impact on the patient's quality of life.

To this end the GDG posed 3 questions that aimed to provide the evidence for effectiveness and safety of VLCDs as well as establishing what maintenance strategies maximised weight loss in the long-term. Each of these questions and the evidence are presented in this chapter. The GDG interpretation of the body of evidence considered, together with recommendations made, conclude the chapter. This guidance amended the definition of VLCD to ≤ 800 calories per day in line with current practice, whereas the previous guideline had used a definition of 1000 calories or less. The search for this review question was repeated without any date cut-offs to ensure that no relevant evidence was missed.

7.2 Review question: In people who are overweight or obese, what is the clinical and cost effectiveness of very-low-calorie diets in reducing weight?

For full details see review protocol in Appendix C.

Table 7: PICO characteristics of review question

Population	Adults (18 years old and over) Children (over 2 years)
Intervention(s)	Very-low-calorie diet (≤800 calories per day) – these should be nutritionally complete. Includes intermittent diets (for example VLCD meal replacements just 2 days a week –

	which may follow a period of daily VLCD (usually 8 weeks and then intermittent)).
Comparison(s)	Standard dietary advice defined as: low-calorie (regular) diet (LCD) 800-1600 calories per day or 500/800 deficit diet.
Outcomes	• % weight in kg change (from start of study to end of maintenance period) • Health related quality of life • Withdrawals • Weight in BMI, change (from start of study to end of maintenance period) - % reduction IMPORTANT • Weight change at end of VLCD to end of maintenance period - % kg • Weight change at end of VLCD to end of maintenance period - % BMI • Improvement in physical activity
Study design	RCT or systematic review of RCTs.

7.2.1 Clinical evidence

Seven studies were included in the review.[51,63-65,67,68,70] Evidence from these studies is summarised in the clinical evidence summary below (Table 8). See also the study selection flow chart in Appendix D, study evidence tables in Appendix G, forest plots in Appendix I, GRADE tables in Appendix O and excluded studies list in Appendix J.

Three studies reported on specific populations: 1 with all male participants in an occupational setting [51] and 2 with all female participants.[64,65] Furthermore, 3 studies reported on people with type 2 diabetes. [63,67,70]

All included studies compared VLCD to standard dietary advice, but the length of VLCD (8-50 weeks), the number of calories included (400-800 kcals), and the length of treatment and follow-up (6 months-24 months), varied. Three papers[63,64,68] reported intermittent VLCD. Six studies [51,64,65,67,68,70] included behavioural therapy (or educational sessions) as part of the treatment in both arms and 4 of these studies included an exercise component as well.[51,64,65,70]

No studies reported the weight change outcomes in the GDG preferred units of percentage loss of initial weight. However, the studies did report BMI or kg change so this was used instead. One study did report percentage 'ideal' weight loss, which was included.[51]

None of the studies reported weight change (BMI or kg) from end of VLCD to end of maintenance period. However, studies reported weight change from start of study to end of VLCD and from start of study to end of maintenance period which indirectly provided the same information, so this was reported instead.

Numbers of participants withdrawing from the study was extracted for all 7 studies. None of the included studies reported on the following outcomes from the protocol: health -related quality of life and improvement in physical activity.

Table 8: Summary of studies included in the review

Study	Intervention/comparison	Population	Outcomes	Comments
Pavlou 1989[51]	**Treatment (8 weeks)** Randomly assigned to 1 of 4 diet groups, and either exercise (90 min supervised, 3 times a week) or non-exercise group VLCD + exercise (n= 57): • DPC-70, a 420 kcal powdered protein-carbohydrate mix • DPC-800, an 800 kcal diet provided in powder form Standard dietary advice + exercise (i.e. LCD, n= 53) • Balanced caloric-deficit diet, 1000 kcal • Protein-sparing modified fast, ~1000 kcal All participants attended weekly educational sessions **Follow-up 6 + 18 months**	Moderately obese men (22% above ideal body weight), 26-52 yr. Initial weight: Treatment 101.9 kg (4.585) Comparator 101.5 kg (3.853)	% weight loss ('ideal') Withdrawals Weight in kg, change (start of study to end of maintenance period)	All male sample Combined VLCD and LCD groups have comparable baseline weights. However, separate groups had wide range (96.1 – 105.7 kg) Unclear follow-up period "final weight", assume 18 month follow-up Measure of physical activity, unable to extract data in any useful way
Simonen 2000[63]	**Run in (6 weeks)** Participants consumed an ad libitum diet at home **Treatment (3 months)** VLCD (n= 10): • Daily 3 servings of a VLCD (97 kJ/d, Cambridge diet; Howard Foundation, Cambridge, UK – 14.2 g protein, 15.0 g carbohydrates, 2.7 g fat) Standard dietary advice (i.e. LCD, n= 6)	Obese (>30 BMI) patients with recently diagnosed (<2yr) T2D Initial weight: All participants 93.2 kg (3.74)	Withdrawals Weight in kg, change (start of study to end of maintenance period)	Small sample Unclear calorie total in either arm (GDG noted that VLCD was likely to be 97 kJ/d per kilo) Serum and metabolic variables were not significantly different between treatment groups,

Study	Intervention/comparison	Population	Outcomes	Comments
	• Advised to consumed a low-fat, low-cholesterol diet **Weight maintenance diet (up to 2 years)**			therefore, participants were analysed in aggregate – results taken from HTA
Viegener 1990[64]	**Treatment (6 months)** Behavioural therapy + exercise + diet (intermittent diet, n= 42): • VLCD - 800 kcal/day, low fat diet, used 4 days a week (3 days: 1200 kcal/day) Behavioural therapy + exercise + diet (standard deficit diet, N= 43) • 1200 kcal/day Treatment also included exercise component (i.e. programmed aerobic exercise, target goal 30 minutes per day, 6 days a week) During treatment, participants received 26 weekly group sessions, each 2 hours in duration **Weight maintenance (6 months)** During maintenance, participants undertook therapist-led "maintenance" sessions, held twice a month	Females, 21-59 years of age, 25-99% overweight (based on the height-weight tables of the Metropolitan Life Insurance Company, 1983) Initial weight: Treatment 98.6 kg (15.9) Comparator 94.6 kg (12.6)	Withdrawals Weight in kg, change (start of study to end of VLCD period) Weight in kg, change (start of study to end of maintenance period)	All female sample Difference in baseline weight Intermittent VLCD
Wadden 1994[65]	**Treatment (52 week programme + 26 week follow-up)** Behavioural therapy + exercise + short-term use of a VLCD (n = 28): • Week 1: 1200 kcal/day • Week 2-17: liquid formula VLCD (OPTIFAST 70, provided 420 kcal/day (70 g protein, 30 g	Obese women, mean age 39 years, 106.33 kg, 39.46 BMI Recruited by newspaper advertisements seeking persons at least 25 kg	Withdrawals Weight in kg, change (start of study to end of VLC period) Weight in kg, change	All female sample Short-term VLCD (16 weeks) Assuming numbers at end of treatment, i.e. week 17 (report number of

Study	Intervention/comparison	Population	Outcomes	Comments
	carbohydrate, 2 g fat)) • Week 8-23: conventional foods gradually reintroduced and amount of liquid formula reduced so that by week 23 consuming 1000 kcal/day diet of conventional foods • Week 24-52: consume conventional reducing diet of 1200 kcal/day Behavioural therapy + exercise + a balanced-deficit diet (n= 21) • 1200 kcal/day • 15-20% of calories derived from protein, no more than 30% from fat, and the remainder from carbohydrates Participants in both conditions began exercise program at week 8, which mostly consisted of walking (exercise for 10-20 min, 2-3 times a week, at 40-60% of estimated maximum heart rate – by week 52: 20-40 min, 3-5 times a week, 60-70% maximum heart rate) All participants participated in weekly group treatment sessions for first 52 weeks (instruction in traditional behavioural methods of weight control, e.g. controlling stimuli associated with eating, slowing the rate of eating, etc.) and biweekly sessions for an additional 26 weeks (6-9 participants, 90 min)	overweight, as determined by the height-weight tables of the Metropolitan Life Insurance Company (1983). Initial weight: Treatment 107.85 kg (14.89) 40.01 (5.73) Comparator 105.43 kg (13.68) 38.80 BMI (5.39)	(start of study to end of maintenance period)	participants at week 9, 26, and 78) % weight loss from fat, at 17 weeks: VLCD (n= 16) -72.11 (11.06) BDD (n= 15) -81.75 (53.75)
Wing 1984[68]	**Pre-treatment assessment (10 days)** **Treatment (10 weeks)** Intermittent low-calorie regimen (i.e. VLCD, N= 25): • Given individualised goals to follow for 5 days/week.	Obese participants, age 20-65, ≥20% overweight Initial weight: Treatment 91.8 kg (13.4)	Withdrawals Weight in kg, change (start of study to end of VLCD period)	15 month study Weekly meetings for 10 weeks, each lasting 60-90 minutes; consisting of weigh-in, review, and collection of

Study	Intervention/comparison	Population	Outcomes	Comments
	• For the other 2 days, participants advised to practice 'self-control' by restricting intake to below 750 kcal/day Standard behavioural condition (i.e. LCD, N= 23) • Goal (based on initial weight x 12 – 1000 kcal) of at least 1000 kcal/day **Booster sessions (6 months)** Massed (4 of the 6 meetings held during the third month) or spaced (6 x monthly intervals) booster sessions **Follow-up (6 months)**	Comparator 92.9 kg (18.5)	Weight in kg, change (start of study to end of maintenance period)	food diaries Intermittent VLCD Results combined: VLCD (massed + spaced groups) LCD (massed + spaced
Wing 1991[70]	**Treatment 20 weeks** Behavioural therapy + exercise (n= 19) • 1000-1500 kcal/d Behavioural therapy + exercise + VLCD (n= 17) • 4-week LCD (1000-1500 kcal) • 8-week VLCD (400 kcal/d) • 4 weeks of gradual introduction of other foods • 4-week LCD (1000-1500 kcal) Weekly meetings – included instruction of diet, exercise and behaviour modification Exercise goals – increase walking and given weekly exercise goals, starting at 210 J/week (equivalent to walking 0.5 mile for a 67.5 kg person) and increasing to 4200 J/week (approx 10 miles per week) **Weight maintenance (52 weeks)**	10 men/26 women, 35-70 years of age, 30% or more above ideal body weight, type 2 diabetes Initial weight: BT alone 104.5 kg (21.5) 38.10 BMI (5.7) VLCD 102.1 kg (11.7) 37.34 BMI (4.7)	Withdrawals Weight in kg, change (start of study to end of VLCD treatment) Weight in kg, change (start of study to end of maintenance period) Weight in BMI, change (start of study to end of maintenance period) Weight in BMI, final (start of study to end of maintenance period)	

Study	Intervention/comparison	Population	Outcomes	Comments
Wing 1994[67]	**Treatment 50 weeks** Behavioural therapy + diet (N= 48) • 1000-1200 kcal/d Behavioural therapy + VLCD (N= 45) • Week 1-12: 400-500 kcal/d • Week 13-23: increase to 1000-1200 kcal/d • Week 24-36: 400-500 kcal/d • Week 37-48: increase to 1000-1200 kcal/d Behavioural treatment (weekly group meetings) occurred over 1 year. Meetings consisted of individual weigh-in, review of self-monitoring records, and a lecture and discussion concerning a topic related to nutrition, exercise or behaviour modification.	Obese patients with T2D (diagnosis of diabetes for an average of 6.8 years [SD 6.2]) Initial weight: VLCD 105.8 kg (19.4) 37.42 BMI (6.13) Standard dietary advice 107.7 kg (18.7) 38.31 BMI (6.52)	Withdrawals Weight in kg, change (start of study to end of VLCD period) Weight in kg, change (start of study to end of maintenance period) Weight in BMI, change (start of study to end of VLCD period)	

Table 9: Summary of studies included in the review: weight in kg

Study	Mean kg – baseline	Mean kg – end of VLCD period	Mean kg – end of weight maintenance period
Pavlou 1989	VLCD: 101.9 kg (4.585) LCD: 101.5 kg (3.853)	8 weeks: Unable to extract data from graph	18 months: VLCD: 89.8 kg (5.56) LCD: 90.77 kg (4.281)
Simonen 2000	Overall: 93.2 kg (3.7)	12 weeks: Unable to extract data from paper	24 months: Overall: 87.2 kg (3.2)
Viegener 1990	VLCD: 94.6 kg (12.6) Standard diet: 98.6 kg (15.9)	26 weeks: VLCD: -10.2 kg (5.1) [84.4 kg] Standard diet: -8.9 kg (5.6) [89.7 kg]	12 months: VLCD: -9.0 kg (6.7) [85.6 kg] Standard diet: -8.9 kg (7.3) [89.7 kg]
Wadden 1994	VLCD: 107.85 kg (14.89 Standard diet: 105.43 kg (13.68)	17 weeks: VLCD: -20.50 kg (7.29) [87.35 kg] Standard diet: -9.14 kg (6.17) [96.29 kg]	18 months: VLCD: -10.94 kg (9.97) [96.91kg] Standard diet: -12.18 kg (8.23) [93.25 kg]
Wing 1984	VLCD: 91.8 kg (13.4) Standard diet: 92.9 kg (18.5)	10 weeks: VLCD: -8.4 kg (1.4) [90.96 kg] Standard diet: -7.8 kg (1.5) [85.1 kg]	12 months: VLCD: -2.7 kg (2.4) [89.1 kg] Standard diet: -3.0 kg (2.3) [89.9 kg]
Wing 1991	VLCD: 102.1 kg (11.7) Standard diet: 104.5 kg (21.5)	20 weeks: VLCD: 83.5 kg (9.5) Standard diet: 94.4 kg (19.8)	12 months: VLCD: 93.5 kg (10.4) Standard diet: 97.7 kg (17.4)
Wing 1994	VLCD: 105.8 kg (19.4) Standard diet: 107.7 kg (18.7)	52 weeks: VLCD: -14.2 kg (10.3) [91.6 kg] Standard diet:-10.5 kg (11.6) [97.5 kg]	24 months: VLCD: -7.2 kg (8.0) [98.6 kg] Standard diet: -5.7 kg (7.9) [102 kg]

Table 10: Summary of studies included in the review: withdrawals

Study	Baseline	End of VLCD period	End of weight maintenance period	Explanation for withdrawals	Other measures of adherence
Pavlou 1989	Treatment: n= 80 Comparator: n= 80	8 weeks: Not specified	18 months: Treatment: n= 57 Comparator: n= 53	None given	
Simonen 2000	Treatment: n= 10 Comparator: n= 6	12 weeks: Paper reports no withdrawals	24 months: Paper reports no withdrawals	Not applicable	
Viegener 1990	Treatment: n= 42 Comparator: n= 43	26 weeks: Treatment: N= 31 Comparator: N= 32	12 months: Treatment: n= 30 Comparator: n= 30	Paper states "conservative assumption of assuming that each client who dropped out of treatment had relapsed to pre-treatment weight…". No other details given.	Attendance at treatment group sessions and twice a month maintenance sessions Self-reported adherence to behavioural weight loss strategies
Wadden 1994	Treatment: n= 28 Comparator: n= 21	17 weeks: Treatment: N= 28 Comparator: N= 21 *assumption	18 months Treatment: n= 21 Comparator: n= 16	Reasons reported overall only: of 12 who dropped out overall (including 3 during maintenance), 2 were because of illness or death in the family, 1 moved, 1 started a job conflicting with treatment, but the rest felt that they did not have time for the program or were unhappy with their weight losses or both	Withdrawals reported at: week 9 (VLCD: n= 28, LCD: n= 21)* week 26 (VLCD: n= 26, LCD: n= 17) week 52 (VLCD: n= 23, LCD: n= 17) week 78 (VLCD: n= 21, LCD: n= 16) Treatment sessions: Attendance high in both condition during first 26 weeks, averaging 24.03 visits Fell during next 26 weeks to a mean of 17.76 Attendance during weeks 53-78 was low in both conditions, averaging

Study	Baseline	End of VLCD period	End of weight maintenance period	Explanation for withdrawals	Other measures of adherence
					only 6.51 of 13 possible visits.
Wing 1984	Treatment: n= 25 Comparator: n= 23	10 weeks: Treatment: n= 24 Comparator: n= 22	12 months: Treatment: n= 23 Comparator: n= 21	Paper states "the 2 dropouts (1 from each condition) were assumed to have lost no weight". No other details given.	Number of days participants reported eating <750 kcal during 10 week treatment Number of weeks participants reported eating <750 kcal for 2 days/week during 10 weeks. Total calorie intake
Wing 1991	Treatment: n= 17 Comparator: n= 19	20 weeks: Treatment: n= 17 Comparator: n= 16	72 weeks: Treatment: n= 17 Comparator: n= 16	None given	Self-monitoring records of caloric intake Eating behaviour
Wing 1994	Treatment: n= 45 Comparator: n= 48	52 weeks: Treatment: n= 38 Comparator: n= 41	24 months: Treatment: n= 36 Comparator: n= 37	None given	Attendance

Table 11: Clinical evidence profile: VLCD versus standard dietary advice for overweight and obese people

Outcome	Number of studies	Imprecision	GRADE rating	Absolute Difference	Control event rate (per 1000)	Control event rate for continuous outcomes
% (ideal) weight loss	1	Serious	Very low	MD 2.1% higher (3.4 lower to 7.6 higher)	-	65.4%
Health related quality of life	0	-	-	-	-	-
Withdrawals	7	Serious	Very low	32 fewer per 1000 (from 85 fewer to 41 more)	229 per 1000	-
Weight in kg, change (from start of study to end of VLCD period)	5	Serious	Very low	MD 4.3 kg lower (5.99 lower to 2.62 higher)	-	-9.14 kg
Weight in kg, change (from start of study to end of weight maintenance period)	7	None	Low	MD 0.96 kg lower (1.66 to 0.25 lower)	-	-6.8 kg
Weight in BMI, change (from start of study to end of VLCD period)	2	Serious	Low	MD 2.09 BMI lower (3.29 to 0.9 lower)	-	-3.69 BMI
Weight in BMI, final (from start of study to end of weight maintenance period)	1	Serious	Very low	MD 1.26 BMI lower (4.17 to 1.65 lower)	-	35.4 BMI

7.2.2 Economic evidence

7.2.2.1 Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

7.2.2.2 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

The sections below detail the costs borne by the NHS for providing a VLCD diet. These costs have been calculated in conjunction with GDG members who have experience in running VLCDs services within NHS weight loss management programmes and therefore reflect what is seen in current NHS led VLCD programmes. Note that the level of care provided as part of a VLCD varies across the UK, therefore the following costs are intended to provide only an example of the costs faced; local costs will vary. This analysis focuses on NHS-run VLCDs, though consideration is given to commercially run VLCDs. Two cost analyses were conducted:

- VCLDs that individuals with and without comorbidities with a BMI over 40 kg/m^2 may receive.
- VLCDs that individuals with no comorbidities and a BMI 30 - 40 kg/m^2 may receive.

Tier 3 service VLCD costs (individuals with and without comorbidities with a BMI over 40 kg/m^2)

The following represents the costs per individual for undertaking a VLCD for 1 year. Where appropriate, separate costs are displayed for individuals with comorbidities, such as hypertension and type-2 diabetes. These individuals are likely to receive a different level of care to ensure their comorbidities are properly monitored and controlled.

Initial medical assessment

When an individual first undertakes a VLCD they undergo an initial assessment in which their suitability is assessed, and they receive advice on how to undertake the diet properly. The individual is also discussed at a separate multidisciplinary-team (MDT) meeting which comprises of medical professionals who will be involved in the VLCD. The costs of these assessments are shown in Table 12.

Table 12: Initial medical assessment

Item	Description	Cost	Source
Medical consultant assessment	1 x 45 minute assessment	£74	GDG estimate, PSSRU[12]
Dietitian (band 7) assessment[(a)]	1 x 30 minute assessment	£24	GDG estimate, PSSRU[12], NHS pay and conditions circular[46]
Blood tests and time taken to review results[(b)]	Including: FBC, Ues, LFTs, bone, Vit D, iron studies, B12, folate, fasting lipids and HbA1c.	£178	GDG estimate, PSSRU[12]
10 minute MDT	1 x dietitian 1 x psychologist 1 x physiotherapist 1 x medical consultant	£41	GDG estimate, PSSRU[12]

(a) In some centres this assessment may be completed by a clinical nurse specialist instead; however the cost difference is small
(b) This is based on the assumption that it takes 5 minutes for a medical consultant to review blood results

Undertaking the diet

After the initial medical assessment the individual undergoes the diet for 12 weeks. During this period they are likely to receive intense monitoring to identify any medical or compliance issues. Individuals with comorbidities are likely to receive additional monitoring from different healthcare professionals to ensure their comorbidities are being correctly treated. They may also receive additional telephone support from a clinical nurse specialist. Monitoring costs for individuals with no comorbidities are shown in Table 13, and monitoring costs for individuals with comorbidities are shown in Table 14.

Table 13: Costs of undertaking the diet for individuals with no comorbidities

Item	Description	Cost per assessment	Cost	Source
Monitoring	12 x 30 minute assessments with dietitian (band 7)	£24	£288	GDG estimate, PSSRU[12], NHS pay and conditions circular[46]

Table 14: Costs of undertaking the diet for individuals with comorbidities

Item	Description	Cost per assessment	Cost	Source
Monitoring	2 x 30 minute assessments with physician; 2 x 30 minute assessments with CNS; 8 x 30 minutes with dietitian	£50 per physician appointment £26 per CNS appointment £24 per dietitian appointment	£344	GDG estimate, PSSRU[12], NHS pay and conditions circular[46]
CNS monitoring during 12 weeks the individual is on the diet	17 x 15 minute phone calls[(a)]	£13 per phone call	£221	GDG estimate, PSSRU[12]

(a) Once every other day in the first 2 weeks, then once a week until the diet is complete.

End of programme

After the diet has been completed the individual will have their blood tested again and undertake a final medical assessment to discuss a follow-up plan. It is assumed that if the individual has comorbidities then this final assessment will take place with a medical consultant, the costs of which are shown in Table 15. If the individual has no comorbidities then the final assessment takes place with a dietitian, the costs of which are shown in Table 16.

Table 15: Final medical assessment for individuals with comorbidities

Item	Description	Cost	Source
Medical consultant assessment	1 x 60 minute assessment	£99	GDG estimate, PSSRU[12]
Blood tests and time taken to review results	Including: FBC, Ues, LFTs, bone, Vit D, iron studies,	£178	GDG estimate, PSSRU[12]

Item	Description	Cost	Source
	B12, folate, fasting lipids and HbA1c		

Table 16: Final medical assessment for individuals with no comorbidities

Item	Description	Cost	Source
Dietitian assessment (band 7)	1 x 60 minute assessment	£48	GDG estimate, PSSRU[12], NHS pay and conditions circular[46]
Blood tests and time taken to review results	Including: FBC, Ues, LFTs, bone, Vit D, iron studies, B12, folate, fasting lipids and HbA1c	£178	GDG estimate, PSSRU[12]

Follow-up

It is assumed that after the diet the individual will continue to receive regular monitoring, in the form of monthly follow-up visits with a dietitian, to ensure weight is maintained and any medical issues are identified and addressed. These costs are shown in Table 17.

Table 17: Follow-up

Item	Description	Cost per appointment	Cost	Source
Follow-up visits	9 x 30 minute assessments with dietitian (band 7)	£24	£216	GDG estimate, PSSRU[12], NHS pay and conditions circular[46]

Additional costs

During the time the VLCD is being undertaken there are additional pressures placed on NHS services to accommodate people undertaking a VLCD. This includes additional time spent by an administrator and longer MDT meetings. Individuals on a VLCD will be seen more and therefore more time will be spent by an administrator making appointments, entering additional information into a database and sending more letters to the individual's GP. MDT meetings are weekly meetings which are used to discuss the progress and issues of patients on the service, and individuals who are undertaking a VLCD will require more time to discuss any safety or compliance concerns. Individuals with comorbidities will have an even longer MDT discussion to discuss issues related to medication titration for example. The additional costs for patients with no comorbidities are shown in Table 18, and the additional costs for patients with comorbidities are shown in Table 19. Note that transport costs have been excluded from this analysis as most services do not cover transport costs and this cost is not specific to VLCDs.

Table 18: Additional costs borne by the centre for individuals with no comorbidities

Item	Description	Cost per week	Cost	Source
Additional 5 minutes a week at MDT for the twelve weeks the individual is undertaking the	Individuals involved in MDT: 1 x dietitian 1 x psychologist 1 x physiotherapist	£21	£246	GDG estimate, PSSRU[12]

Item	Description	Cost per week	Cost	Source
VLCD	1 x medical consultant			
Additional 15 minutes a week for twelve weeks for additional database entry work	Band 4 administrator	£7	£78	GDG estimate, NHS pay and conditions circular[46]

Table 19: Additional costs borne by the centre for individuals with comorbidities

Item	Description	Cost per week	Cost	Source
Additional 10 minutes a week at MDT for the twelve weeks the individual is undertaking the VLCD	Individuals involved in MDT: 1 x dietitian 1 x psychologist 1 x physiotherapist 1 x medical consultant	£41	£491	GDG estimate, PSSRU[12]
Additional 15 minutes a week for twelve weeks for additional database entry work	Band 4 administrator	£7	£78	GDG estimate, NHS pay and conditions circular[46]

The comparator

In this analysis VLCDs are compared to a tier 3 weight management service. This decision was made given that:

- The majority of people placed on VLCDs in the NHS are those already on a tier 3 weight management service
- These individuals have a BMI over 40 kg/m^2, therefore they are likely to receive intensive treatment.

Some of the costs detailed above would be incurred as part of a tier 3 weight management service, even if the patient had not gone on the VLCD. The cost components that are unique to a VLCD are identified in the following section.

Incremental costs

The incremental cost of providing a VLCD in comparison to a tier 3 weight management service is calculated in Table 20. This assumes:

- After 1 year people who underwent a VLCD will receive the same standard of care as those on a tier 3 service.
- People undertaking a VLCD will also receive the level of care provided within a tier 3 service, for example the same number of physiotherapist and psychologist visits.

Table 20: Incremental costs for undertaking a VLCD

Item	Cost
Additional time spent at MDT	£246

Item	Cost
Additional time taken to complete database	£78
Additional 5 hours of dietitian time (assuming a standard tier 3 service would provide 7 hours of dietitian time per year).	£240
Blood tests	£356
Initial medical assessment by medical consultant	£74
Additional costs for individuals with comorbidities: 2 additional hours with medial consultant, 5.25 hours with CNS, additional 5 minutes per week at MDT however 3 hours less with dietitian.	£573
Total for patients with no comorbidities	**£994**
Total for patients with comorbidities	**£1567**

Sensitivity analysis

To reflect the differential level of care patients may receive, sensitivity analyses were run on the costs by considering the following additional scenarios.

Firstly, in some centres, an MDT may not be run to discuss individuals with no comorbidities on a VLCD. Instead, medical support may be offered to these patients if they choose to access it. An assumption was made, based on GDG opinion, that 20% of individuals would access this additional medical support. The cost of this additional support is calculated in Table 21, and would be instead of the additional MDT cost calculated in Table 18 for people with no comorbidities. For people with comorbidities it was assumed in this sensitivity analysis that the MDT would last the same amount of time as in a tier 3 service.

Table 21: Cost of additional medical support

Item	Description	Cost	Source
Additional medical support	12 x 30 minute assessments with a medical consultant for 20% of patients	£40	PSSRU[12], GDG estimate

Secondly, in some centres, blood tests may also be taken for people as part of the tier 3 service, and therefore do not represent an incremental cost.

Table 22: Incremental costs for undertaking a VLCD (low end estimate)

Item	Cost
Additional medical support (no MDT)	£40
Additional time taken to complete database	£78
Additional 5 hours of dietitian time (assuming a standard tier 3 service would provide 7 hours of dietitian time per year).	£240
Initial medical assessment by medical consultant	£74
Additional costs for individuals with comorbidities: 2 additional hours with medial consultant, 5.25 hours with CNS, however 3 hours less with dietitian.	£327
Total for patients with no comorbidities	**£432**
Total for patients with comorbidities	**£759**

Primary care VLCD costs (individuals without comorbidities with a BMI 30 – 40 kg/m^2)

The GDG also recognised that a small group of individuals with a BMI between 30 – 40 kg/m^2 with no comorbidities may receive a much less intensive care package during their VLCD. These individuals would only receive an initial medical assessment from a dietitian, then weekly monitoring visits during the time the individual is on the diet. They would have access to medical support, provided by a GP, and an assumption was made that only 20% of patients would access this service. The costs of this service are provided in Table 23.

Table 23: Costs of reduced care package VLCD in people with no comorbidities

Item	Description	Cost	Source
Initial medical assessment	1 x 60 minute visit with band 5 dietitian	£31	GDG estimate, PSSRU[12]
Monitoring during the diet	12 x 30 minute visits with dietitian (band 5)	£186	GDG estimate, PSSRU[12]
Medical support	30 minutes with GP assuming 20% of patients access this service	£19	GDG estimate, PSSRU[12]
Total		£236	

As these people will not require intense treatment the relevant comparator is standard dietary advice. This consists of visits with a dietitian the costs of which are provided in Table 24.

Table 24: Cost of standard dietary advice

Item	Description	Cost	Source
Initial visit	1 x 60 minute band 5 dietitian appointment	£31	GDG estimate, PSSRU[12]
Follow-up	3 x 30 minute dietitian appointments	£47	GDG estimate, PSSRU[12]
Total		£78	

Therefore the incremental costs of providing a VLCD for these people is £158.

Commercially run VLCD

A number of people choose to fund their own VLCD and complete this outside of NHS care. Even though the individual pays for the service, there are still costs borne by the NHS. These costs are mainly relevant to individuals with comorbidities and are related to medical assessments that are required by the commercial providers before and during the diet. The NHS will incur the cost of a professional assessment to ensure the VLCD is safe to complete and also the cost professional monitoring via telephone to alter medication and ensure no complications arise. Finally, the costs of any adverse effects that arise from undertaking the VLCD will also fall on the NHS.

Economic considerations

Using the incremental cost of providing a VLCD, the QALY increase which would be required for VLCDs to be considered cost effective at a £20,000 per QALY threshold can be calculated like so:

$$Change\ in\ QALYs = \frac{Change\ in\ cost}{£20{,}000}$$

The change in BMI required to achieve this increase in QALYs can then be calculated using data on the health related quality of life (HRQoL) increase expected from a 1 point reduction in BMI:

$$BMI\ change\ needed = \frac{Change\ in\ QALYs}{HRQoL\ increase\ per\ one\ unit\ reduction\ in\ BMI}$$

Evidence from the literature[17,34] suggests that HRQoL increases between 0.0079- 0.0164 per unit decrease in BMI. Therefore if a unit decrease in BMI was sustained for a year this would mean an increase of 0.0079 – 0.0164 QALYs. It is worth noting that the estimate of 0.0164, derived from Dixon et al,[17] is unadjusted for age and whether or not the individual has type-1 or type-2 diabetes. The estimate of 0.0079, derived from Lee et al,[34] is for non-diabetics and adjusted for age. Therefore we would expect the true value to be closer to 0.0079 for patients without diabetes.

Using the information above, the BMI changes needed for VLCDs to be cost effective at a £20,000 per QALY threshold are displayed in Table 25 taking into account the range of costs and quality of life values.

Table 25: BMI change needed for VLCD to be cost effective at a £20,000 per QALY threshold (no comorbidities)

Cost/Effect	0.0079 (lower estimate for quality of increase per BMI unit change)	0.0164 (upper estimate for quality of increase per BMI unit change)
£432 (lower estimate for tier 3 VLCD)	2.73 kg/m^2	1.32 kg/m^2
£994 (Base case estimate for tier 3 VLCD)	6.29 kg/m^2	3.03 kg/m^2
£158 (Cost for primary care VLCD)	1 kg/m^2	0.48 kg/m^2

Literature suggests that the HRQoL improvements associated with BMI reductions may be higher for individuals with type-2 diabetes (T2D).[34] Using the T2D specific estimate detailed in Lee et al,[34] Table 26 details the BMI change needed for VLCDs to be cost effective at a £20,000 per QALY threshold for individuals with T2D.

Table 26: BMI change needed for VLCD to be cost effective at a £20,000 per QALY threshold (people with T2D)

Cost/Effect	0.01 (lower estimate for quality of increase per BMI unit change)	0.0164 (upper estimate for quality of increase per BMI unit change)
£759 (lower estimate for tier 3 VLCD)	3.80 kg/m^2	2.31 kg/m^2
£1567 (Upper estimate for tier 3 VLCD)	7.84 kg/m^2	4.78 kg/m^2

Other considerations:

A study by Lean et al[32] calculated the costs of running a low-energy-liquid-diet of 810–833 kcal/day and found the cost to the NHS to be £861 per patient. To be comparable with the above analysis, by excluding the costs of the formula diet, Orlistat and the costs to Counterweight, this cost falls to £266 per patient. However this cost is averaged across all individuals that entered the study. Due to drop-out rates the cost of an individual that completed the diet would likely be higher. As the study's exclusion criteria is fairly strict the individuals who completed the diet in the study are unlikely to represent those seen in a tier 3 service, therefore these costs are more comparable to the costs

calculated for primary care run VLCDs above. It is worth noting that that the healthcare staff participating in the study were already familiar with the counterweight programme in Scotland. This means their skills would not be representative of current skill levels in primary care in the rest of the UK. This would affect the amount of time staff would spend with the individual on the VLCD and therefore the cost of the intervention. Finally although the calorie intake just falls above this guideline's definition of 800 kcal/day for a VLCD the GDG noted that the costs could still be relevant. With all things considered, this study suggests that the £236 cost calculated in Table 23 could be seen as an underestimate of the true cost of the intervention to the NHS.

Secondly, this analysis only considers the costs associated with the VLCD, and only HRQoL changes associated with weight change. In reality the probability of a person experiencing comorbidities is likely to decrease as they lose weight. By reducing these comorbidities the individual will achieve a higher HRQoL, for example weight loss may improve osteoarthritis related knee pain or improve obesity related sleep apnoea, and costs to the NHS will fall. For example reducing BMI results in lower prescriptions costs as outlined in a study by the counterweight project team.[10] The study showed that unit BMI decreases from 40 kg/m^2 can reduce prescription costs by £5 - £8 per year.

Thirdly, in this analysis, the HRQoL increases per unit change in BMI reflect an assumed linear relationship between BMI and HRQoL. A study by Hunger et al[22] shows that HRQoL is sensitive to changes in BMI between 30 – 40 kg/m^2 however is fairly unresponsive to changes between a BMI of 40 – 45 kg/m^2. If the weight change from a VLCD was the same for all BMI values then this analysis would suggest that they are less likely to be cost effective for individuals with a BMI above 40 kg/m^2.

Finally the above analysis does not take into account any adverse effects that could arise from a VLCD. These could reduce HRQoL and increase costs to the NHS.

7.2.3 Evidence statements

7.2.3.1 Clinical

- Low to very low quality evidence showed that there may be no clinical difference between VLCD and standard dietary advice in:
  - % ideal weight loss (1 study, n=110)
  - Withdrawals (7 studies, n=487)
  - Weight in BMI change from start of study to end of weight maintenance period (1 studies, n=33)
  - Weight in kg change from start of study to end of weight maintenance period (7 studies, n=373)

- However, low to very low evidence showed that there may be a clinical benefit for VLCD in:
  - Weight in kg change from start of study to end of VLCD period (5 studies, n=265)
  - Weight in BMI change from start of study to end of VLCD period (2 studies, n=112)

- No evidence was found for health related quality of life outcome.

7.2.3.2 Economic

- No relevant economic evaluations were identified.
- An original comparative cost analysis showed that:
  - For obese individuals with comorbidities:

- Using the lowest cost estimate for VLCDs and the highest quality of life estimate for unit decreases in BMI, a VLCD would need to reduce BMI by 2.31 kg/m^2 and sustain this for 1 year, to be considered cost effective at a £20,000 per QALY threshold.
- Using the highest cost estimate for VLCDs and the lowest quality of life estimate for unit decreases in BMI, a VLCD would need to reduce BMI by 7.84 kg/m^2 and sustain this for 1 year, to be considered cost effective at a £20,000 per QALY threshold.
- For obese individuals without comorbidities:
- Using the lowest cost estimate for VLCDs and the highest quality of life estimate for unit decreases in BMI, a VLCD would need to reduce BMI by 0.48 kg/m^2 and sustain this for 1 year, to be considered cost effective at a £20,000 per QALY threshold.
- Using the highest cost estimate for VLCDs and the lowest quality of life estimate for unit decreases in BMI, a VLCD would need to reduce BMI by 6.29 kg/m^2 and sustain this for 1 year, to be considered cost effective at a £20,000 per QALY threshold.
- This analysis was considered directly applicable with potentially serious limitations.

7.2.4 Review question: In people who are overweight or obese, what is the safety of very-low-calorie diets when used to reduce weight and maintain weight loss?

For full details see review protocol in Appendix C.

Table 27: PICO characteristics of review question

Population	Overweight or obese people
Intervention(s)	Very-low-calorie diet (≤800 calories per day)
Comparison(s)	Standard dietary advice: - low-calorie diet (>800-1600 calories per day) - 500-800 calorie deficit diet
Outcomes	Critical: 1. Disordered eating at latest follow up 2. Depression score at latest follow up 3. Postural hypotension at latest follow up Important: 4. Bone density at latest follow up 5. Constipation at latest follow up 6. Gall stones at latest follow up 7. Gout at latest follow up 8. Diarrhoea at latest follow up 9. Hypoglycaemia at latest follow up
Study design	RCT or systematic review of RCTs

7.2.5 Clinical evidence

Six studies were included in the review.[4,8,9,20,56,65,66,69] These are summarised in Table 28 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 29). See also the study selection flow chart in Appendix D, study evidence tables in Appendix G, forest plots in Appendix I, GRADE tables in Appendix O and excluded studies list in Appendix J.

Mean BMI ranged between 31.9 and 39 kg/m^2 in most studies[4,8,9,20,56,65,69] but 1 study [66] had mean BMI of 40 and 44 kg/m^2 in VLCD and LCD arms, respectively. Two studies reported on specific populations: one on participants with type 2 diabetes,[69] and another on participants with osteoarthritis.[8,9,56]

All included studies compared VLCD to LCD but the length of VLCD varied (from 8 to 12 weeks) as well as the number of calories included (ranging from 400-520 kcal/d). The range of calories included for a LCD varied from 810 kcal/d to 1500 kcal in 1 study. The studies also varied in whether or not the VLCD treatment period included some time on a LCD (before or after the VLCD).

Furthermore, 4 [8,9,56,65,66,69] studies included behavioural therapy as part of the treatment in both arms and 2 of these studies included exercise as well.

One study reported on binge eating scores (with the Binge Eating Scale), 1 aspect of disordered eating scale [65]. However, no studies reported on other aspects of disordered eating such as night eating syndrome and bulimia nervosa.

Three studies[65,66,69] reported final depression scores on Beck's Depression Inventory at different time points ranging from 4 months to 1 year. Since depression scores were expected to be different sooner after treatment when patients have achieved the most weight loss (18 weeks as in one study) than at 1 year when they may have gained back some weight (as in another study), results were presented separately for different time points.

One study[8,9,56] reported the proportion of people with depressive tendencies at the end of the study but it was not clear how many of these individuals had depressive tendencies at the start of the study.

One study each reported on gallstones[20], uric acid levels (gout)[4], diarrhoea[8,9,56], and constipation[8,9,56] (an additional study [69] reported levels of uric acid but only in the VLCD group).

However, none of the included studies reported comparative data from the following outcomes from the protocol: postural hypotension, bone mineral density, or hypoglycaemia.

Table 28: Summary of studies included in the review

Study	Intervention/comparison	Length of intervention (length of follow-up)	Population	Outcomes	Comments
Arai 1992[4] Japan	-4 to 8 week VLCD (419 kcal) (n=20) - 4 to 8 week LCD (839-1199 kcal) (n=25)	4-8 weeks	Obese adults (n=45) Mean BMI: 37 kg/m^2 (SD 4) VLCD 36 kg/m^2 (SD 6) LCD	Serum uric acid Marked serum uric acid (dichotomous)	No details on whether patients also received behavioural treatment. No comment on the incidence of clinical gout.
Gebhard 1996[20] USA	-12-week VLCD (520 kcal) (n=6) -12-week LCD (900 kcal) (n=7) (both were then gradually transitioned from liquid to solid 1000 kcal/d at 18 weeks and 1500 kcal/d at 24 weeks)	24 week program	Obese adults (n=13) Mean BMI: 37 kg/m^2 (SD 4) VLCD 36 kg/m^2 (SD 6) LCD	Gallstones (dichotomous)	24-week program included weekly meetings, diary and compliance review by an experienced dietitian and periodic evaluation by a physician.
CAROT study (Rieke 2010[56] and Christensen 2011[8,9]) Denmark	-8-week VLCD (415 kcal) (n=96) -8-week LCD (810) (n=96) (+behavioural therapy for both) (both followed by 8-week LCD [1200 kcal/d])	16 weeks	Obese adults with knee osteoarthritis (n=192) Mean BMI: 37.3 kg/m^2 (SD 4.8, range 30.1-54)	Constipation (dichotomous) Depression tendencies (dichotomous) Diarrhoea (dichotomous)	Nutritional instructions and behaviour therapy by an experienced dietitian at weekly sessions through 16 weeks (1.5 hours).
Wadden 1990[66] USA	1200 kcal/d for 4 weeks then randomisation to: -8-week VLCD (400-500 kcal/d) then 10-week LCD (1200 kcal/d) -18-week LCD (1200 kcal/d) (+behavioural therapy for both)	18 weeks	Obese women (n=15) Mean BMI: 40.7 kg/m^2 (SD 10) VLCD 44.6 kg/m^2 (SD 9) LCD	Depression score (continuous)	Behavioural therapy consisted of weekly group sessions (1.5 hours) of 4-7 subjects led by a doctoral-level clinical psychologist.

Study	Intervention/comparison	Length of intervention (length of follow-up)	Population	Outcomes	Comments
Wadden 1994[65] USA	-12-week VLCD (420 kcal/d) then LCD (1200 kcal/d) for 48 weeks -52-week LCD (1200 kcal/d) (+ behavioural therapy and exercise programme for both)	52 weeks (+26 weeks follow-up)	Obese women (n=49) Mean BMI: 39.46 kg/m^2 (40.01 kg/m^2 [SD 5.73] VLCD, 38.80 kg/m^2 [SD 5.39] LCD)	Binge eating score (an aspect of disordered eating) (continuous)[a] Depression score (continuous)[a]	Behavioural therapy consisted of weekly group sessions 6-9 subjects led by a doctoral-level clinical psychologist or a psychology graduate student. Exercise programme started at week 8; it consisted mostly of walking (increase from 10-20 minutes for 2-3times/wk to 20-40 min 3-5 times/wk at week 52).
Wing 1991[69] USA	-20-week VLCD program: - 4-week LCD (1000-1500 kcal) - 8-week VLCD (400 kcal/d) - 4 weeks of gradual introduction of other foods - 4-week LCD (1000-1500 kcal) -20-week LCD (1000-1500 kcal/d) (+ behavioural therapy and exercise for both)	20 weeks (+1 year follow-up)	Obese adults with type 2 diabetes (n=36) Mean BMI: 37.34 kg/m^2 (SD4.7) VLCD 38.10 kg/m^2 (SD 5.7) LCD	Depression score (continuous)[b] Levels of uric acid 'Marked' uric acid levels[c]	Behavioural therapy consisted of weekly group sessions for the treatment period led by a team of therapists around diet, exercise and behaviour modification. Exercise was recommended and subjects given weekly goals (starting from 210 J/wk [~50 kcal] to 4200 J/wk [~1000 kcal]). No subjects developed clinical symptoms of gout. Only 1 patient had a uric acid level greater than 594 umol/L.

(a) These outcomes were only reported at 52 weeks of treatment (not after the additional 26-weeks of follow-up)
(b) The study states that the outcome was reported at '4 and 5 months' (not otherwise explained)
(c) Unclear how this was defined in the study

Table 29: Clinical evidence summary: VLCD versus LCD (both with or without behavioural and/or exercise therapy) for overweight and obese people

Outcome	Number of studies	Imprecision	GRADE rating	Absolute Difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Binge eating a	1	Serious	Very low	MD 6.32 higher (1.68 to 10.96 higher)	n/a	12
Depression score at 4 to 5 months b, c (continuous)	2	Very serious	Very low	MD 2.03 lower (11.09 lower to 7.03 higher)	n/a	5.95
Depression score at 1 year b (continuous)	1	Serious	Very low	MD 3.32 higher (1.22 lower to 7.86 higher)	n/a	5
Depressive tendencies (dichotomous)	1	Very serious	Very low	36 more per 1000 (from 16 fewer to 238 more)	34 per 1000	n/a
Postural hypotension	-	-	-	-	-	-
Constipation	1	Very serious	Very low	45 more per 1000 (from 73 fewer to 230 more)	281 per 1000	n/a
Gall stones	1	Serious	Low	670 more per 1000 (from 270 fewer to 1060 more)	0 per 1000	n/a
Serum uric acid (continuous)	1	Serious	Very low	MD 23.6 lower (72.17 lower to 24.97 higher)	-	306.8 µmol/L
'Marked' d serum uric acid concentration	1	Serious	Very low	350 more per 1000 (from 140 higher to 560 higher)	0 per 1000	-
Diarrhoea	1	Very serious	Very low	13 more per 1000 (from 23 fewer to 170 more)	34 per 1000	n/a

(a) One aspect of disordered eating which was the outcome specified in the protocol (no other data found); measured with Binge Eating Scale

(b) Beck's Depression Inventory
(c) Includes a study reporting this outcome at 18 weeks and another at '4 to 5 months'; the later appears to be an average of results through these months
(d) The level considered 'marked' was not described in study

7.2.6 Economic evidence

See review on the effectiveness of VLCD for economic evidence.

7.2.7 Evidence statements

7.2.7.1 Clinical

- VLCDs may result in more binge eating after 1 year compared to LCDs (1 study, n=45, very low quality).
- It is unclear if depression is worse after VLCDs than after LCDs (3 studies, n=100, very low quality).
- There were more participants with 'depressive tendencies' after VLCDs than after LCDs (1 study, n=192, very low quality).
- Constipation (1 study, n=192, very low quality) and diarrhoea (1 study, n=192, very low quality) may be more frequent after VLCDs than LCDs.
- Gallstones occurred in some people during or after VLCDs but not with LCDs; however this was only symptomatic in 1 individual (1 study, n=13, low quality).
- There were similar serum uric acid levels in VLCDs and LCDs; however, more participants with VLCDs had 'marked' increases in serum uric acid at some point during treatment but these were not correlated with episodes of gout (1 study, n=45, very low quality).
- There was no evidence on postural hypotension, bone density, or hypoglycaemia.

7.2.7.2 Economic

- No relevant economic evaluations were identified.

7.2.8 Review question: What are effective management strategies for maintaining weight loss after very-low-calorie diets in people who are overweight or obese?

For full details see review protocol in Appendix C.

Table 30: PICO characteristics of review question

Population	Adults (18 years old and over) Children (over 2 years)
Intervention(s)	All participants have a lead-in period on a very-low-calorie diet (VLCD; ≤800 kcal) for 6-12 weeks before randomisation. Intervention: maintenance strategy: • Anti-obesity drugs • Exercise • Diet • Behavioural therapy • Combinations of above
Comparison(s)	Standard dietary advice (control) Placebo Other maintenance strategies
Outcomes	% weight change (kg) from end of VLCD to end of study Health related quality of life Withdrawals % change in body mass index (BMI) from end of VLCD to end of study

	% weight change from before VLCD to end of study (kg) % change in BMI from before VLCD to end of study Improvement in physical activity
Study design	RCT or systematic review of RCTs

A minimum study duration of 1 year was required for study inclusion because that was considered necessary to assess long-term maintenance of weight loss.

7.2.9 Methods summary

The protocol included a range of interventions (behavioural therapy, anti-obesity drugs, diet), which should not be combined in a meta-analysis and were reported separately. The protocol also treated separately comparisons with no treatment and placebo.

The various interventions were clustered into 6 main comparisons:

1. behavioural therapy and different re-feeding techniques [Agras 1996]
2. hypocaloric diet (1600 kcal/day), with additional 238 kcal VLCD diet (total 1838 kcal/day) [Ryttig 1997] or including VLCD sachet (total 1600 kcal/day) [Ryttig 1995]
3. dietary counselling with exercise versus dietary counselling only [Borg 2002, Fogelholm 2000]
4. Orlistat with or without dietary and lifestyle counselling versus dietary and lifestyle counselling or meal replacement [LeCheminant 2005, Richelsen 2007]; and, Orlistat with dietary and lifestyle counselling versus dietary and lifestyle counselling only [Richelsen 2007]
5. high protein diet versus high carbohydrate diet [Delbridge 2009]
6. interventions compared to no treatment: Sertraline versus placebo [Wadden 1995], high protein diet versus no treatment [Lejeune 2005], fibre diet versus no treatment [Pasman 1997]

The duration of VLCD varied from 1 to 6 months and this may influence the effectiveness of maintenance regimens. Similarly, the length of maintenance regimen and follow-up also varied (1 year was inclusion criteria, maintenance ranged up to 3 years).

The protocol specified the outcomes, % weight change (kg) from end of VLCD to end of study and % change in body mass index (BMI) from end of VLCD (called 'baseline') to end of study. The GDG considered as alternative outcomes, the weight at the end of the study or the weight change from before VLCD to the end of study or from the end of VLCD to the end of study. The GDG considered the outcomes in relation to the weight at baseline (that is, at the end of VLCD), end of treatment and end of follow-up. Another protocol outcome was withdrawals at baseline, end of treatment and end of follow-up. It was important to distinguish between withdrawals due to maintenance strategy or due to other circumstances.

In addition to the forest plots for each individual pairwise comparison, 2 forest plots summarising all comparisons in the literature were presented to the GDG: 1 including all head-to-head trials and 1 including all trials with interventions against either no treatment or no placebo.

7.2.10 Clinical evidence

10 papers were included in the review.[2,5,13,19,33,35,50,55,58,59]

4 studies reported on sub populations: 3 with all female participants (Agras 1996, Fogelholm 2000, and Pasman 1997) and 1 with male participants (Borg 2002). Furthermore, 5 studies did not have a minimum weight loss for inclusion in the maintenance phase of the study. There were differences in weight (kg) at baseline between treatment arms; for example, Ryttig 1995 reported a 12 kg difference between the 2 separate intervention arms.

Only 1 study reported the protocol % change outcomes,[50] and the rest reported the alternative outcomes. Most studies reported withdrawals from maintenance; however, it was often unclear whether they were withdrawals due to maintenance strategy or due to other circumstances. None of the included studies reported on health-related quality of life. Two studies reported physical activity as an outcome [5,19] but as both studies were exercise interventions and this outcome was only reported during the study, the results are more about adherence to the exercise regimen rather than improved physical activity after the maintenance programme had completed.

Table 31: Summary of studies included in the review

Study	Intervention/comparison	Population	Outcomes	Comments
Agras1996[2]	Weight loss phase: 3 months, 800 kcal (n=201) Included in maintenance if ≥5% weight loss Randomised into one maintenance strategy (n= 194): • behaviour therapy + standard food re-feeding (time dependent) • behaviour therapy + standard food re-feeding (weight dependent) • behaviour therapy + pre-packaged re-feeding (time dependent) • behaviour therapy + pre-packaged re-feeding (weight dependent)	Overweight women (unclear definition)	Weight change in kg, withdrawals	All had concurrent behaviour therapy (modifying their own food intake, increased physical activity levels, eating slower) weekly for first 3 months, fortnightly for the next 3 months and then monthly for the last 3 months of treatment.
Borg2002[5]	Weight loss phase: 2 months: 1 week LCD 1200, 6 week VLCD 500, 1 week LCD 1200 (n=90) (no minimum weight loss for inclusion in maintenance reported) Randomised into one maintenance strategy (n= 82): • dietary counselling + walking • dietary counselling + resistance training • control (dietary counselling)	Men (BMI >30 kg/m^2), between 35-50 year	Weight in kg (final value, adjusted ANCOVA), withdrawals	All patients attended weekly meetings in small groups where problems with diet and prevention of relapses were discussed. Patients were instructed to follow a low-fat and high carb diet. They received written educational material monthly.
Delbridge2009[13]	Weight loss phase: 3 months, ~500-550kcal (n= 180) Included in maintenance if ≥10% weight loss Randomised into one maintenance strategy (n= 141): • High protein diet • High carbohydrate diet	Obese patients (BMI ≥30 or ≥27 with comorbidities), ≥18-to ≤75 yr	Weight change from before VLCD to end of weight maintenance period (kg), weight change (kg) from end of VLCD period to end of weight maintenance period, withdrawals	Both groups advised to reduce fat intake to <30% of their intake, monthly counselling sessions, encouraged to practice healthy behaviours such as aerobic exercise ≥3 times/wk.

Study	Intervention/comparison	Population	Outcomes	Comments
Fogelholm2000[19]	Weight loss phase: 2 months: 1 wk LCD 1200, 6 wk VLCD 500, 1 wk LCD 1200 (n= 85) (no minimum weight loss for inclusion in maintenance reported) Randomised into one maintenance strategy (n= 82): • dietary counselling + exercise (target 1000kcal) • dietary counselling + exercise (target 2000kcal) • control (dietary counselling)	Pre-menopausal women (BMI 30-45 kg/m^2), between 30-45 yr	Weight in kg (final value), adjusted ANCOVA), withdrawals	
LeCheminant2005[33]	Weight loss phase: 3 months: 520 kcal (n= 157) (no minimum weight loss for inclusion in maintenance reported) Randomised into one maintenance strategy (n= 147): • Meal replacement • Orlistat	Overweight or obese (≥28 BMI), 19-70 yr	Weight in kg (final score), withdrawals	
Lejeune2005[35]	Weight loss phase: 1 months: ~500 kcal (n= 140) Included in maintenance if 5-10% weight loss Randomised into one maintenance strategy (n= 120): • Protein • Control	Moderately overweight (25-35 BMI), 18-60 yr	Weight change (kg), withdrawals	
Pasman1997[50]	Weight loss phase: 2 months: ~477 (n= 48) Included in maintenance if >5kg body weight Randomised into one maintenance strategy (n= 41): • Fibre diet • No treatment (control)	Obese female (no further details of inclusion)	Weight in kg (final score), weight in BMI (final score), withdrawals	
Richelsen2007[55]	Weight loss phase: 8 wk, 600-800 kcal (n= 383) Included in maintenance if >5% weight loss	Obese (BMI >30 and <45), 18-65 yr	Weight change from start of study to end	Instructed to follow a standard energy-restricted diet (600 kcal

Study	Intervention/comparison	Population	Outcomes	Comments
	Randomised into one maintenance strategy (n= 309): • Dietary and lifestyle counselling with orlistat • Dietary and lifestyle counselling with placebo		of weight maintenance period (kg), weight change (kg) from end of VLCD period to end of weight maintenance period, withdrawals	daily deficit) during maintenance phase. Dietitian provided dietary and lifestyle counselling. Advised to reduced fat to ~30% of total energy and engage in daily physical activity.
Rytigg1995 [59]	Weight loss phase: 3 months, 330 kcal (n= 114) (no minimum weight loss for inclusion in maintenance reported) Randomised into one maintenance strategy (n= 60): • Hypocaloric diet (1600 kcal) with VLCD (220 of the 1600 kcals) • Standard hypocaloric diet (1600 kcal)	Obese (>30 BMI), 19-65 yr	% weight change from start of study to end of weight maintenance period (kg), weight in kg (change score), withdrawals	Standard hypocaloric diet group had higher baseline weight, both before VLCD (120.1 (22.5) vs. 108.1 (15.8)) and after VLCD (97.6 (19.1) vs. 85.7 (14.7)).
Rytigg1997[58]	Weight loss phase: 2 months, 420 kcal (n= 81) (no minimum weight loss for inclusion in maintenance reported) Randomised into one maintenance strategy (n= 81): • Hypocaloric diet (1600 kcal) with VLCD (238 kcals) • Standard hypocaloric diet (1600 kcal)	Obese (≥30 BMI), 21-64 yr	% weight change from start of study to end of weight maintenance period (kg), weight in kg (final score), withdrawals	

Table 32: Summary of studies included in the review: weight in kg

Study	Mean kg - baseline	Mean kg – end of VLCD period	Mean kg – end of weight maintenance period
Agras 1996	Baseline, overall: • 100.3 kg (14) • 36.6 BMI (4.4)	After treatment, 12 weeks: • time-dependent regular food condition: -15.2 kg (4.8, n= 47) • weight-dependent regular food condition: -15.0 (4.8 n= 45) • time-dependent stimulus narrowing condition -14.9 (4.5, n= 38) • weight-dependent stimulus narrowing condition: -14.2 (4.1, n= 44)	Last follow-up, 18 months: • time-dependent regular food condition: -8.2 kg (12.3, n= 45) • weight-dependent regular food condition: -8.6 (11.8, n= 41) • time-dependent stimulus narrowing condition -6.0 (11.1, n= 34) • weight-dependent stimulus narrowing condition: -2.8 (18.3, n= 42)
Borg 2002	Baseline: • All: 106.0 kg (9.9)	At 8 weeks (post lead-in): • All: 91.7 kg (9.4) • Control: 92.3 kg (10.5) • Walking: 91.9 kg (9.3) • Resistance: 90.8 kg (8.6)	At 8 months (post intervention): • Control: 99.9 kg (11.1) • Walking: 93.7 kg (10.7) • Resistance: 91.1 kg (8.0)
Delbridge 2009	Baseline: • Treatment HC: 109.4 kg (2.6) • Comparator HP: 114.0 kg (3.0)	After 12 week lead-in: • All: -16.5 kg (0.5) • Treatment HC: -17.6 kg (0.8) [91.8 kg] • Comparator HP: -17.4 kg (0.7) [96.6 kg]	12 month follow-up: • Treatment HC: -14.3 kg (2.0) [95.1 kg] • Comparator HP: -14.8 kg (1.5) [99.2 kg]
Fogelholm 2000	Baseline: • All: 92.0 kg (9.8) (weight loss after 12 week weight reduction phase was 13.1 kg (3.5))	Start of weight maintenance program: • Control: 80.0 kg (9.5) • Walk 1: 78.0 kg (8.8) • Walk 2: 78.2 kg (11.6) End of weight maintenance program (40 weeks): • Control: 82.0 kg (10.2) • Walk 1: 77.3 kg (10.7) • Walk 2: 77.6 kg (11.1)	End of follow-up (24 months): • Control 89.7 kg (9.6) • Walk 1: 83.9 kg (12.2) • Walk 2: 87.4 kg (15.3)
Lejeune	Baseline:	After 26 week weight maintenance:	Weight loss at 6 month follow up:

Study	Mean kg - baseline	Mean kg – end of VLCD period	Mean kg – end of weight maintenance period
2005	• Protein: 83.1 kg (11.1) • Carbohydrate: 83.4 kg (10.4) After 4 week VLED: • Protein: 76.7 kg (9.9) • Carbohydrate: 77.3 kg (9.9)	• Protein: 77.5 kg (11.8) • Carbohydrate: 80.3 kg (11.6)	• Protein: -5.5 (0.9) [77.6 kg] • Carbohydrate: -2.6 (1.2) [80.8 kg] (calculated from graph)
LeCheminant 2005	Weight loss from baseline to end of 16 week VLCD: • Meal replacement: -22.8 kg (6.1) • Orlistat: -22.3 kg (6.1) (from text, actual baseline weights not reported)	At week 16, randomisation to treatment arm: • Meal replacement: 85.4 kg (14.3) • Orlistat: 85.7 kg (17.9)	12 months, end of treatment: • Meal replacement: 88.1 kg (16.5) • Orlistat: 88.5 kg (20.3)
Pasman 1997	Baseline: • All: 88.7 kg (10.4) • Fibre: 88.4 kg (9.559) • Control: 89.4 kg (12.6)	End of VLCD, 8 weeks: • Fibre: 77.95 kg (8.429) • Control: 78.3 kg (10.6)	End of study, 14 months: • Fibre: 87 kg (11.78) • Control: 85.0 kg (12.0)
Richelsen 2007	Baseline: • Orlistat: 110 kg (75-162) • Placebo: 112 kg (78-152)	End of VLED, 8 weeks: • Placebo: -14.3 kg (12) [95.7 kg] • Orlistat: -14.5 kg (13) [97.5 kg]	36 month follow-up: • Placebo: -7.2 kg (6.3) [102.8 kg] • Orlistat: -9.4 kg (8.3) [102.6 kg]
Ryttig 1995	Baseline: • All: 112.4 kg (19.8) • Hypocaloric diet: 108.1 kg(15.8) • Control: 120.1 kg (22.5)	Start of weight maintenance (12 week VLCD): • Hypocaloric diet: 85.7 kg (14.7) • Control: 97.6 kg (19.1)	End of weight maintenance (12 months): • Hypocaloric diet: +8.0 kg (8.2) • Control: +12.3 kg (9.7)
Ryttig 1997	Baseline: • Hypocaloric diet: 116.2 kg (21.0) • B) VLCD run in, hypocaloric only & C) VLCD run in, hypocaloric, plus VLCD: 113.2 kg (17.7)	VLCD run in (8 weeks): • Hypocaloric diet: 109.0 kg (18.9) • B) VLCD run in, hypocaloric only & C) VLCD run in, hypocaloric, plus VLCD: 94.0 kg (13.9)	End of the programme (26 months): • Hypocaloric diet: 110.7 kg (17.4) • VLCD run in, hypocaloric only: 107.3 kg (15.1) • VLCD run in, hypocaloric, plus VLCD: 107.5 kg (16.9)

Table 33: Summary of studies included in the review: withdrawals

Study	Baseline	End of VLCD period	End of weight maintenance period	Explanation for withdrawals	Other measures of adherence
Agras 1996	Entered study, n= 201 6 dropped during run in VLCD 1 did not meet entry criteria (i.e. 5% reduction)	n= 194 (stratified on BMI and % weight loss during VLCD and allocated to 1 of 4 groups) • 12 dropped during treatment	Post-treatment, n= 182 • 5 dropped during follow-up • incomplete data, n= 3 Final n= 174	Of the 17 dropped post-randomisation: • time-dependent regular food condition • weight-dependent regular food condition • 7 time-dependent stimulus narrowing condition • weight-dependent stimulus narrowing condition	Attendance at treatment sessions post-randomisation, 3-month reintroduction of food phase, and treatment.
Borg 2002	Completed weight reduction phase (2 months), n= 90	Completed weight maintenance phase (6 months), N= 82 • Control: n= 29 • Walking: n= 25 • Resistance: n= 28	Measured at the end of follow-up (23 months), N= 68 • Control: n= 22 • Walking: n= 20 • Resistance: n= 26	Due to lack of time or interest None due to illness or injuries related to the intervention program. No difference in dropout rates between study groups.	Physical activity Energy intake (food diary)
Delbridge 2009	Entered study, n= 180 During 3-month lead-in: • 1 failed screening criteria (diagnosis of hemochromatosis •	Started 12 month treatment, n= 141 • High Carbohydrate: n= 70 • High Protein: n= 71	High Carbohydrate: n= 40 • 29 withdrew • 1 did not proceed (decided not to continue after randomisation)		Compliance with dietary recommendations assessed with food diaries and by the objective measures of urea excretion and weight maintenance Attrition

Study	Baseline	End of VLCD period	End of weight maintenance period	Explanation for withdrawals	Other measures of adherence
	• 14 failed to lose ≥10% body weight • 4 lost ≥10% body weight but withdrew		High Protein: n= 42 • 26 withdrew • 3 excluded (poor compliance with protocol; did not attend a sufficient number of study visits)		
Fogelholm 2000	Entered study, n= 85 • dropped during 12 week weight reduction run in Randomised to 40 week weight maintenance phase, n= 82 • Control: 29 • Walk 1: 26 • Walk 2: 27	Completed 40 week program, n= 80 • Control: 28 • Walk 1: 25 • Walk 2: 27	Completed 2 year follow up, n= 74 • Control: 27 • Walk 1: 24 • Walk 2: 23		
Lejeune 2005	n= 140 recruited to study • 20 did not start study due to relocation, a change of job or inability to fulfil schedule • 7 dropped out because of difficulty maintaining the diet n= 113 began 4 week	Randomised to weight maintenance phase, 6 months, n= 113 • Protein: n= 53 • Carbohydrate: n= 60	Follow-up, 6 months, n= 70 • Protein: n= 31 • Carbohydrate: n= 39	No reason given for drop of 43 participants between entering weight maintenance phase and end of follow-up	

Study	Baseline	End of VLCD period	End of weight maintenance period	Explanation for withdrawals	Other measures of adherence
	VLCD run-in • No report of dropouts				
LeCheminant 2005	Enrolled in the study, 12 week VLED, n= 157 • Meal replacement: N= 90 • Orlistat: N= 67	Randomised at week 16, n= 147 • Meal replacement: N= 86 • Orlistat: N= 61	Completed all testing (36 weeks treatment), at week 52, n= 92 • Meal replacement: N= 56 • Orlistat: N= 36	Failure to comply with study protocol, job-related conflicts, illness, and injury not related to the investigation.	Prescribed number of meal replacements: • Women: 121 per week (86%) • Men: 16.1 per week (>100%) Prescribed medication: • Women: 12.6 pills per week (90%) • Men: 13.4 pills per week (96%)
Pasman 1997	Entered study, n= 48 Completed the 2 month VLCD run-in: n= 41 • 7 unable to follow the strict VLCD regime Entered the treatment phase, n= 39 • 2 lost less than 5kg of body weight	Randomly assigned to treatment arm, n= 39 Fibre supplement, n=25 Non-treatment group, n= 14 • 1 not able to come for test at month 10 • 1 became pregnant • 1 spinal cord operation • 5 dropped out due to personal circumstances	Completed treatment (complete data for), n= 31	Total drop, n= 17	Compliance of fibre intake (questionnaire): • Consumed more than 80% of supplement amount of fibre, n= 10 • Consumed between 50-80% of required fibre, n= 10 • Control, n= 11
Richelsen 2007	Met eligibility criteria and started VLED treatment, n= 383	Achieved ≥5% weight loss after 8 weeks VLED, n= 309 • Orlistat: n= 153 • Placebo: n= 156	No specific mention of how many participants completed the treatment and had data at follow-up (36 months).		Premature withdrawals were similar in the orlistat (33.3%) and the placebo group (37.2%) during the 3-year trial.

Study	Baseline	End of VLCD period	End of weight maintenance period	Explanation for withdrawals	Other measures of adherence
Ryttig 1995	Entered study, n= 60 Failed to complete VLCD (12 weeks), n= 8 (all female) • became pregnant • could not accept the VLCD and discontinued after 6 weeks • 2 did not show up • 1 became depressed • 1 hospitalised due to myocarditis • (also, during VLCD, due to severe hunger feelings, 2 patients received transiently one extra sachet of the Cambridge diet per day)	Entered study, n= 52 Discontinued prematurely (5 females, 2 males), n= 7 • became pregnant • 1 due to a gastroplastic obesity operation • 4 did not show up	Completed trial, n= 45 Hypocaloric diet with VLCD, n= 23 Control, n= 22		Compliance: 75% of all patients remained in the whole 64-week programme.
Ryttig 1997	Started study, n= 81 • Hypocaloric diet: n= 27 • B) + C) VLCD run-in, n= 54 • VLCD run-in: • Hypocaloric only: n= 27 • C) Hypocaloric, plus VLCD: n= 27	-	Completed treatment, n= 42 • Hypocaloric diet: n= 16 • Hypocaloric only: n= 11 • C) Hypocaloric, plus VLCD: n= 15	4 patients in the VLCD groups discontinued the treatment prematurely during the first two months: 2 due to side-effects of the VLCD preparation 1 moved abroad 1 due to epileptic seizure not related to the	-

Study	Baseline	End of VLCD period	End of weight maintenance period	Explanation for withdrawals	Other measures of adherence
				treatment 39 patients discontinued the treatment before the 2-year follow-up (note – number completed and number discontinued do not match. Figures as reported in paper)	

Table 34: Clinical evidence summary: head-to-head trials

			Weight in kg			Withdrawals		
Comparison	**Number of studies**	**Length of maintenance period + follow-up**	**GRADE rating**	**Absolute Difference (GRADE rating)**	**Control quantity**	**GRADE rating**	**Withdrawals: Absolute Difference (GRADE rating)**	**Control event rate (per 1000)**
Time dependent re-feeding vs. weight dependent re-feeding (all with behavioural therapy) (after 3 month VLCD)	1[2]	9 months maintenance + 6 month follow-up	Very low	MD 0.9 higher (3.11 lower to 4.9 higher)	2.8 or 8.6 kg	Very low	77 fewer per 1000	72 per 1000
Standard vs. pre-packaged re-feeding (all with behavioural therapy) (after 3 month VLCD)	1[2]	9 months maintenance + 6 months follow-up	Very low	MD 3.59 higher (0.47 lower to 7.65 higher)	6 or 2.8 kg	Very low	77 fewer per 1000	129 per 1000
Dietary counselling + exercise (1000 kcal or 2000 kcal burn) vs. dietary counselling only (after 3 month VLCD)	1 (but 2 arms) [19]	~9 months maintenance + 24 month follow-up	Very low	MD 4.25 lower (9.59 lower to 1.08 higher)	89.7 kg	Very low	43 more per 1000	69 per 1000
Dietary counselling + exercise (1200 kcal or resistance) vs. dietary counselling only (after 2 month VLCD)	1 (but 2 arms)[5]	6 months maintenance + 23 months follow-up	Very low	MD 0.02 higher (6.18 lower to 6.22 higher)	100.7 kg	Very low	106 fewer per 1000	241 per 1000
Orlistat vs meal replacement (after 3 month VLCD)	1[33]	~ 8 months maintenance including follow-up	Very low	MD 0.4 lower (8.32 lower to 7.52 higher)	88.5 kg	Very low	83 fewer per 1000	463 per 1000
Orlistat + dietary and lifestyle counselling vs. dietary and lifestyle counselling only (after 2 month VLCD)	1[55]	36 months maintenance including follow-up	Low	MD 2.4 lower (4.16 to 0.64 lower)	7 kg	Moderate	40 more per 1000	333 per 1000

			Weight in kg			Withdrawals		
Comparison	**Number of studies**	**Length of maintenance period + follow-up**	**GRADE rating**	**Absolute Difference (GRADE rating)**	**Control quantity**	**GRADE rating**	**Withdrawals: Absolute Difference (GRADE rating)**	**Control event rate (per 1000)**
Hypocaloric diet (1600kcal) vs. meal replacement diet (1600kcal + 238kcal VLCD) vs. (after 2 month VLCD)	1[58]	24 months maintenance including follow-up	Very low	MD 0.2 lower (12.56 lower to 12.16 higher)	107.5 kg	Low	147 more per 1000	444 per 1000
Hypocaloric diet (1600kcal) including 220 VLCD vs. Hypocaloric diet (1600kcal) (after 3 months VLCD)	1[59]	12 months maintenance including follow-up	Very low	MD 3 lower (7.92 lower to 1.92 higher)	12.3 kg	Very low	92 more per 1000	69 per 1000
High protein vs high carbohydrate (after 3 month VLCD)	1[13]	12 months maintenance	Low	MD 1.3 lower (1.85 to 0.75 lower)	4.3 kg	Very low	83 fewer per 1000	463 per 1000

Table 35: Clinical evidence summary: intervention versus no treatment

			Weight in kg			Withdrawals		
Comparison	**Number of studies**	**Length of maintenance period + follow-up**	**GRADE rating**	**Absolute Difference (GRADE rating)**	**Control quantity**	**GRADE rating**	**Withdrawals: Absolute Difference (GRADE rating)**	**Control event rate (per 1000)**
Fibre vs no treatment (after 2 months VLCD)	1[50]	14 months maintenance including follow-up	Very low	MD 2 higher (6.77 lower to 10.77 higher)	85 kg	Very low	15 fewer per 1000	214 per 1000
High protein diet (18-20% of energy/day) vs no treatment (after 1 month VLCD)	1[35]	6 months maintenance + 6 months follow-up	Low	MD 2.9 lower (3.39 to 2.41 lower)	-2.6 kg	Low	67 more per 1000	350 per 1000

7.2.11 Economic evidence

See review on the effectiveness of very-low-calorie diets for economic evidence.

7.2.12 Evidence statements

7.2.12.1 Clinical

- Behavioural therapy and re-feeding: maintenance strategy did not result in clinical benefit, with greater weight regain (1 study, n= 201, very low quality)
- Orlistat: when compared with both meal replacement and dietary and lifestyle counselling only, the use of orlistat resulted in less weight regain (2 studies, n= 540, moderate to very low quality)
- Dietary counselling with or without exercise: dietary counselling, plus exercise (100 kcal or 200 kcal burn) was a more effective weight loss maintenance strategy than dietary counselling alone (2 studies, n= 175, very low quality)
- Diet, including:
  - Hypocaloric and meal replacement: when compared with a hypocaloric diet only, hypocaloric diet which included a 220 kcal VLCD diet resulted in greater weight loss over the course of the weight maintenance phase; meal replacement (hypocaloric diet, with an additional 238 kcal VLCD) when compared to hypocaloric diet only, resulted in less weight regain also but this was not considered to be of clinical benefit (2 studies, n= 195, low to low quality)
  - High fibre versus no treatment: more weight regain during the high fibre maintenance strategy, when compared to no treatment (1 study, n= 48, very low quality)
  - High protein versus no treatment: less weight regain during the high protein maintenance strategy, when compared to no treatment (1 study, n= 140, low quality)
  - High protein versus high carbohydrate: high protein weight maintenance strategy resulted in great weight loss than the high carbohydrate weight maintenance strategy(1 study, n= 180, very low quality)
- There was no evidence on ‘health related quality of life’ and ‘improvement in physical activity’ outcomes.

7.2.12.2 Economic

- No relevant economic evaluations were identified.

7.2.13 Recommendations and link to evidence

Recommendations	**65. Do not routinely use very-low- calorie diets (800 kcal/day or less) to manage obesity (defined as BMI over 30).[new 2014]** **66. Only consider very-low-calorie diets, as part of a multicomponent weight management strategy, for people who are obese and who have a clinically-assessed need to rapidly lose weight (for example, people who need joint replacement surgery or who are seeking fertility services). Ensure that:** • **the diet is nutritionally complete** • **the diet is followed for a maximum of 12 weeks (continuously or intermittently)** • **the person following the diet is given ongoing clinical support [new 2014]** **67. Before starting someone on a very-low-calorie diet as part of a multi-component weight management strategy:** • **Consider counselling and assess for eating disorders or other psychopathology to make sure the diet is appropriate for them** • **Discuss the risks and benefits with them** • **Tell them that this is not a long-term weight management strategy, and that regaining weight may happen and is not because of their own or their clinician's failure** • **Discuss the reintroduction of food following a liquid diet with them.[new 2014]** **68. Provide a long-term multicomponent strategy to help the person maintain their weight after the use of a very-low-calorie diet. (See recommendation 35).[new 2014]**
Relative values of different outcomes	**VLCD effectiveness** When considering the effectiveness of VLCDs, the critical outcomes which the GDG wished to examine in the literature were % weight change (kg) at end of maintenance period, health related quality of life and withdrawals (to assess adherence). **VLCD safety** The GDG considered that, for the safety of VLCDs, the most critical outcomes which should be examined in the evidence were disordered eating, depression and postural hypotension. They wished to examine the evidence on disordered eating because they were particularly concerned from their clinical experience that the dramatic calorie reduction in diet with VLCD, even though for a short period, may create or worsen pre-existing unhealthy eating patterns, or disordered eating, such as binge eating, bulimia nervosa, or night eating syndrome. They were also particularly concerned to examine the evidence on depression because they noted that depression may be associated with increased weight gain and obesity and may be particularly exacerbated where weight loss and regain occurs over a shorter time period and through more radical changes and adjustments to eating habits such as those involved in the use of VLCD's and following a VLCD. Postural hypotension, if it occurred, was considered to have a significant impact upon an individual's life.

	While it was noted that a proper VLCD with vitamin/mineral supplementation may actually improve a person's vitamin D and iron levels, the GDG identified other important outcomes which may cause a number of problems which they chose to search the evidence for. These were reduction in bone density, constipation, gallstones, gout, diarrhoea, and hypoglycaemia. The GDG felt that reduction in bone density may occur because of insufficient calcium in the diet and may result in fragility and fracture. Constipation, which may be caused by insufficient fibre in the diet, is particularly troubling for individuals and they wished to see if there was evidence to substantiate these concerns. They also wished to see the evidence on the occurrence of gallstones (the result of inactivity of the gallbladder from low fat in VLCD diets) and gout (associated with rapid weight loss) after VLCDs as they considered them to be very painful experiences for people. As gout will be rarely reported, raised serum uric acid levels, which are associated with gout, were felt to be an appropriate surrogate outcome of gout. Diarrhoea, which the GDG thought might occur for several factors including undiagnosed lactose intolerance, was felt to be an important outcome to examine in the literature as it has a significant impact on patients. Hypoglycaemia, while rare, is a serious adverse event that may result from lower energy intake without concomitant review of diabetic medication so they also wanted to examine the incidence in the literature. **VLCD maintenance** The GDG considered, with respect to strategies for maintaining weight loss after VLCD, the most critical outcomes to examine in the literature to be % weight change (kg) from end of VLCD to end of study, health related quality of life and withdrawals. The GDG were particularly interested in looking at weight change from end of VLCD to end of study, because their clinical experience indicated that initial weight loss in people using VLCDs was not sustained.
Trade-off between clinical benefits and harms	The GDG noted the recommendation from CG43 which indicated that the main requirement of a dietary approach to weight loss is that total energy intake should be less than energy expenditure. They also recognised the challenges in engaging people with long-term behavioural change strategies to support and maintain weight loss. Clinicians and people wishing to lose weight may find the benefit offered by immediate and rapid weight loss when adhering to a very-low-calorie diet (a maximum of 12 weeks continuously or intermittently with a low-calorie diet) attractive. The GDG were very much aware that these diets are also available to individuals delivered by the commercial sector (at a cost to the individual). They also noted from their clinical experience that weight regain following a VLCD was common, although weight regain may be slower with proper support in returning to a balanced diet and change in lifestyle. Weight regain in people who have tried VLCDs may cause depression and perpetuate a sense of failure in those people who are trying to manage weight. If weight increases following a VLCD then this would also be undesirable for the person. The GDG noted that this review was an update of the evidence review from the original 2006 guideline but noted that a safety review had previously not been clearly available from the evidence considered in CG43 and wished to identify any concerns associated with such a restricted calorie intake. The GDG noted that early formulations of VLCDs, used in lower BMIs and with limited associated support, had previously been linked to some incidences of mortality in the past. The GDG felt however that the current formulations and associated support made such an outcome unlikely, and therefore did not prioritise this as an outcome in the safety review.

	Gathering and interpreting this evidence would allow the GDG to determine whether the benefit of any rapid initial weight loss, offset against safety and maintenance of weight loss (and consequently any harms), would require any changes to the existing CG43 recommendation for the NHS.
Trade-off between net health benefits and resource use	No relevant economic evaluations were identified. The incremental cost of providing a VLCD relative to a tier 3 service without a VLCD (standard dietary advice) was estimated to be £432 - £994 for individuals without comorbidities and a BMI over 40kg/m^2. This cost increases to £759 - £1567 for individuals with comorbidities. At this cost, individuals without comorbidities would need to reduce their BMI by 1.32 – 6.29 kg/m^2 and sustain this for a year for a VLCD to be considered cost effective at a £20,000 per QALY threshold. Individuals with comorbidities would need to reduce their BMI by 2.31 – 7.84 kg/m^2 and sustain this for a year to be considered cost effective at a £20,000 per QALY threshold. The GDG felt that it was unlikely that this level of weight loss, relative to a tier 3 service without a VLCD, would be achieved or sustained, and therefore agreed that VLCDs are unlikely to be cost effective for this population. They did note that no clinical evidence was available for VLCDs in this population. The GDG did not consider that it was appropriate to extrapolate the effectiveness of a VLCD from one BMI population to another. For individuals with less complex clinical issues (those with no comorbidities and a BMI between 30 – 40 kg/m^2), the incremental costs of using VLCDs are estimated to be lower, with an additional cost of £158 compared to standard dietary advice alone. Using these costs, it was estimated that an individual would need to reduce their BMI by 0.48 – 1 kg/m^2 and sustain this for 1 year for the VLCD to be considered cost effective at a £20,000 per QALY threshold. The clinical evidence showed that at the end of the clinical trials individuals are expected to lose a very small amount of weight relative to standard dietary advice. This small decrease in weight is unlikely to provide any quality of life benefits. Therefore the GDG agreed that it was unlikely that VLCDs would be cost effective in this population at a £20,000 per QALY threshold. The GDG also noted that the small weight loss achieved from a VLCD measured at the end of the clinical studies was unlikely to result in any improvements in comorbidities. Therefore no additional cost savings or health benefits would be realised (note that such additional benefits have not been incorporated into this analysis). The GDG noted that the evidence on adverse events was weak and that there could be other adverse events which would increase costs and reduce quality of life, making VLCDs even less likely to be cost effective. It is assumed that weight loss achieved through the VLCD will have no long-term impact on quality of life unless it is sustained. The GDG felt that, in some cases, rapid initial weight loss may be of increased clinical benefit to some individuals, particularly those who need to meet clinical requirements for further medical or surgical interventions, for example, orthopaedic surgery and fertility treatment. Therefore a VLCD may be cost effective for this group of individuals as there will be a large benefit derived from the rapid initial weight loss which has not been captured in this analysis. For individuals seeking sustained long-term weight loss, the initial fall and then subsequent rise in weight often seen with VLCDs will not offer sustained improvements in quality of life, therefore use of VLCDs is not considered to be cost effective for long-term weight loss.

Quality of evidence	**VLCD effectiveness** The evidence for the effectiveness review was low to very low quality evidence. Evidence was typically downgraded for risk of bias or imprecision. Most of the studies did not report allocation concealment. There were differences in weight (kg) at baseline between treatment arms which would warrant caution when interpreting the weight change outcomes. The GDG felt it important to note that most of these included studies looked at populations with BMIs that the GDG would consider too low to warrant the use of VLCD on the NHS. There was only evidence in some BMI categories and it was not clear that the data would be relevant to the people with higher BMIs who, in practice, are the most likely to be using VLCDs under NHS care. The GDG discussed that there were no recent studies on effectiveness and the most recent was from 2000. It was also noted that 4 of these 6 studies were from the United States which had carefully selected population inclusion and this could lead to selection bias. The outcome weight in kg change from start of study to end of weight maintenance period had heterogeneity but this was explained by sub-grouping studies by intermittent versus non-intermittent VLCD diets. The GDG believed that this was clinically appropriate and sufficiently explained the heterogeneity. No studies reported on percentage weight loss, but one study did report percentage 'ideal' weight loss. Data on weight change in kg and BMI (from start of study to end of VLCD and start of study to end of maintenance period) was extracted and presented to the GDG. Numbers of participants withdrawing from the study were extracted for all 7 studies; however, it was often unclear whether they were withdrawals due to individual patients unable to tolerate the VLCD or due to other circumstances. None of the included studies reported on the following outcomes from the protocol: Health Related Quality of Life and improvement in physical activity. Three studies reported on specific populations: 1 with all male participants and 2 with all female participants. Furthermore, 3 studies reported on people with type 2 diabetes. All included studies compared VLCD to standard dietary advice but the length of VLCD, the number of calories included, the length of treatment, and the length of follow-up, varied. Four papers reported intermittent (3 papers) or short-term (1 paper) use of VLCDs. Six studies included behavioural therapy (or educational sessions) as part of the treatment in both arms, and 4 of these studies included an exercise component as well; however it was not possible to extract any useful data in these areas to inform recommendations. No evidence was found to inform recommendations in the pre-specified subgroups from the protocol: type 2 diabetes, ethnicity, diet and men and women with learning disabilities, people with osteoarthritis, sleep apnoea, and those giving up smoking or BMI thresholds. **VLCD safety** There was very low to low quality evidence on the safety of VLCDs compared to LCDs. Six RCTs were identified which reported on the pre-specified safety outcomes for VLCDs, with many of the outcomes considered critical or important to decision-making only being reported by 1 study. Most of the studies did not report allocation concealment and some included participants with different

baseline characteristics (for example, in depression scores and baseline weight) which may indicate inadequate randomisation or be an indication that allocation was not concealed appropriately. Participants and most of the assessors in the studies did not appear to be blinded and this may have had an impact on the more subjective outcomes, for example depression or binge eating. Furthermore, some of the outcomes such as 'depressive tendencies' and 'marked' serum uric acid levels were not well-defined and the results were very imprecise.

Heterogeneity was found and investigated for the one outcome where meta-analysis was possible: final depression scores at 4 and 5 months. One study[66] which showed higher (worse) depression scores for VLCD than LCD was a very small study and there were problems with using the final values for the later study[69] which reported higher values for VLCD at follow-up. For the later study, baseline values were also higher for VLCD. Consequently, change scores for this study (not reported) are likely to have shown no difference between VLCD and LCD. There was a similar problem with the results in final depression score reported at 1 year [65] where baseline values were also different and, if change scores were reported, may show little difference between VLCD and LCD. Another possible reason for this heterogeneity could be that the study favouring VLCD was reported at 18 weeks follow-up, whereas the studies favouring standard dietary advice were 1 year follow up. The GDG agreed that a period of rapid initial weight loss during the first phase (at 18 weeks) would be more likely to lead to reduced depression, whereas by the later follow-up times, individuals could have experienced weight regain, as they transition to solid food, and would be more likely to have higher depression scores in the VLCD group.

The GDG highlighted that the majority of evidence identified was in an indirect population of people who would be unlikely to receive a VLCD in NHS clinical practice (that is, the evidence is in people with a BMI less than 40). No evidence was identified on the use of VLCDs in people with a BMI over 40 with complex comorbidities.

There was evidence from one study to suggest that binge eating may be worse in those who have VLCD compared to LCD at 1 year. However, the GDG noted that final binge eating scores were better than at baseline; which was considered to be likely due to the psychological support element of the treatment that the patients received. However, there were no outcomes reported related to other aspects of disordered eating, such as bulimia nervosa or night eating syndrome.

Regarding other possible adverse events, one study reported on gallstone formation detected by ultrasound. However, this was a small study which specifically looked at biliary physiology during VLCDs and LCDs and reported a very high rate of (asymptomatic) gallstone formation associated with VLCDs, leading to the study terminating early.

One study reported on constipation and diarrhoea, reporting that there was a slightly higher occurrence of these effects with VLCDs compared to LCDs but there was little certainty in the results.

No studies reported on the occurrence of gout but one small study reported the proportion of participants with 'marked' serum uric acid levels. As the study did not define this, it was difficult to draw any conclusions. The same study reported the mean levels of serum uric acid to be similar between VLCDs and LCDs.

VLCD maintenance

	Most of the evidence for the maintenance review was very low to low quality evidence. The GDG noted that the studies also consisted of small sample sizes. Evidence was typically downgraded for risk of bias or imprecision and outcomes on weight (change or final scores) were downgraded for indirectness as they were not reported in the GDG's preferred way, % change from baseline. Most of the studies did not report allocation concealment. Some outcomes had very wide confidence intervals reflecting large levels of uncertainty in results. There were differences in weight (kg) at baseline between treatment arms. The GDG noted that the evidence presented was not applicable for relevant patients with a BMI above 50 as the majority of the studies included populations with lower BMIs. Only one study presented % change: the remaining studies reported the alternative outcomes. There was no clinical evidence found relating to health related quality of life. It was possible to determine withdrawals for all included studies; however once again, it was often unclear whether they were withdrawals due to the maintenance strategy or due to other circumstances. Two studies reported physical activity as an outcome but as both studies were exercise interventions and this outcome was only reported during the study, the results are more about adherence to the exercise regimen rather than improved physical activity after the maintenance programme had completed. Four studies reported on sub populations: 3 with all female participants and 1 with male participants. Furthermore, 5 studies did not have a minimum weight loss for inclusion in the maintenance phase of the study. No evidence was found to inform recommendations in the pre-specified subgroups (type 2 diabetes: expected weight maintenance strategies following VLCD to have different outcomes in people with T2DM; ethnicity (white (over 80%); Asian (over 80%); black (over 80%): expected maintenance strategies following VLCD to have different outcomes in different ethnicities; learning disabilities; adherence to weight maintenance strategies following VLCD may be challenging for men and women with intellectual disabilities; and, diet: expected weight maintenance strategies involving diet to work better in those who followed a supervised diet) or strata (BMI thresholds - intervention thought likely to have a different effect on different BMI thresholds) in the protocol.
Other considerations	The GDG considered the applicability of these studies and discussed the challenges in maintaining weight loss following any diet including very-low-calorie diets. Overall, the GDG felt that there was little evidence of effectiveness of VLCDs compared to LCDs (standard dietary advice) in the long-term, but they are relatively safe. The GDG noted that there was some evidence that VLCD worked in the short-term, but outcomes for weight loss at end of maintenance periods found no difference between VLCD and standard dietary advice. Evidence demonstrated that VLCDs achieve slightly greater weight loss over the short period of the intervention compared to LCDs; however this loss is not likely to be maintained. This was also supported by evidence to suggest a benefit in weight reduction at the start of a VLCD was not maintained over a long period of time. The GDG noted that the provision of VLCDs is relatively new in the NHS (other than pre-surgery); however they are provided extensively by commercial providers at cost to individuals. It is outside the remit of this guideline to consider issues related to the use of VLCDs purchased by the individual, although the GDG recognise that commercial companies advise their customers to seek medical advice or monitoring in certain conditions (such as hypertension or type 2 diabetes) and as such are not without cost to the NHS as it is usual for people

to get this advice from their NHS general practitioner.

The GDG agreed that VLCDs showed a clinical benefit over harms in the initial phase of the diet but felt that these benefits were rarely evident long-term. They also noted from their experience that many patients regain the weight lost during the initial VLCD period and often end up gaining weight. The GDG discussed the harmful nature of weight cycling and associated morbidity as well as the potential dissatisfaction and sense of failure that this weight regain may cause the individual.

The GDG observed that there was no difference in withdrawals which was being used to determine adherence to the VLCD, and as such were unable to highlight any supportive measures to encourage adherence to any VLCD.

The GDG noted with interest the incidence of gallstones in the VLCD population. The size of this study was acknowledged as a particular weakness, but the GDG were not particularly surprised by the high incidence. It was the opinion of the GDG that gallstones are common after rapid weight loss, but they were unsure whether this was increased in VLCD compared to rapid weight loss by other means. They also noted that they would expect other studies which actively looked for gallstones to discover high rates of gallstones associated with VLCDs. Whilst in practice, their experience demonstrated that the incidence of gall stones in the population was generally increasing probably caused by rapid changes in weight (increase or decrease), there was little evidence to suggest that these were a particular safety issue, especially as, in the evidence reviewed, only one case of gallstones was symptomatic. The GDG also noted that the included study reported using a VLCD with less than 2g of fat per day while the EU SCOOP report62 recommends that there is little risk of gallstones if VLCD include at least 5g per day of fat and virtually no risk with diets that include at least 7g per day. This was considered to be more reflective of current diets. For these reasons, the GDG did not choose to make a research recommendation to further investigate the cause and association and impact of gall stones in the population of people using VLCDs.

The GDG considered the evidence related to depression. While the study showed that those with a VLCD may have higher (worse) depression scores than those with a LCD, scores were also higher in this group at baseline. Given this, the GDG did not feel able to make any conclusions about this.

The GDG did not consider overall that there were benefits to providing VLCDs to the majority of obese people who wish to lose weight and recommended that it should not be routinely offered. However, the GDG considered that there were likely to be some benefits to providing VLCDs to selected people who need to lose weight quickly for clinical reasons, for example, those people who are being considered for surgical procedures such as orthopaedic surgery or women who wish to conceive. The GDG defined 'rapid weight loss' appropriately as greater than that which can be achieved with dietary and lifestyle changes. The GDG recommended the use of VLCDs in patients clinically assessed by the health care professional as likely to benefit from rapid weight loss in these or analogous circumstances. The GDG noted that there is concern that weight loss is not too rapid (that is, likely to result in excess loss of lean body mass and increase risk of gallstones) and that it is important to manage safely. The usual recommendation is 0.5-1kg/week (that is 0.5-1% for a 100kg person). Weight loss may be more rapid in the first couple of weeks due to fluid loss. The GDG noted that the maximum, safe, recommended rate without losing significant lean mass is approximately 1.5% per week, noting that the maximum weight loss per week

required to not exceed this needs to be recalculated as weight is lost. The most successful VLCD trials achieve a total weight loss of 8-12% over 12 weeks which is in keeping with a 1% per week loss.

The GDG reported that from personal experience there is a group of individuals who may do very well on a VLCD despite the poor evidence. The GDG agreed that patient choice would also be very important as some patients may not want to try a VLCD while others would be very keen. They also indicated in their recommendation a set of activities that should take place before a VLCD was offered that reflects the importance of ensuring that people are aware of the challenges with ensuring long-term sustained weight loss with this type of diet. They felt it important to ensure that the use of VLCDs was only used as part of a multicomponent intervention to ensure weight loss (as already recommended in CG43), and chose to highlight this in their recommendations. Furthermore, the GDG considered it important to note that diets less than 800kcal, were carried out under clinical supervision.

The GDG also discussed the evidence related to disordered eating. The GDG felt from their clinical experience that individuals without a previous history of disordered eating behaviours may be more at risk of developing these after use of a VLCD, although no evidence that fit the criteria specified in the protocol was found. They agreed by consensus that careful review and screening of people being considered for a VLCD diet for binge eating and other disordered eating behaviours was necessary as from their clinical experience, VLCDs may trigger these behaviours and they chose to include this specifically in their recommendation. They particularly wished to ensure that the re-introduction of normal or solid food was carefully discussed to ensure that the person was reintroduced to a balanced diet rather than return to previous eating habits to maximise the chance to maintain weight loss following the intervention. Although no formal review of the evidence to identify the support that an individual should receive before initiating a VLCD, they felt that it was important to highlight that individuals being considered for a VLCD as part of a multi component weight strategy should be considered for counselling and assessed for eating disorders and other psychopathology. The GDG recognise that in any service of this kind, an appropriate pathway should be in place. It is beyond the scope of this guideline, however, to define that pathway or which professional groups support any pathway. The GDG noted that, from their tier 3 service experience, relevant psychological skills support, usually from a clinical psychologist, was available for the necessary assessment for eating disorders or similar. The GDG also wished to highlight that a discussion regarding the risks and benefits of VLCDs, and the concept of VLCD as a short-term weight strategy should take place before initiation of the diet. The GDG particularly felt that the re-introduction of healthy eating habits was more likely if the reintroduction of food had been discussed before the start of the diet. The GDG also wished to note that they considered it may also be important to discuss potential side effects and to monitor in order to ensure any side effects are only transient. The GDG used informal consensus to develop a recommendation to reflect this.

The GDG wished to highlight that all people who are being given a VLCD should be monitored and reviewed regularly and provided with support to help maintain weight loss. The duration of this support should be tailored to individual need as outlined in recommendation 38.

The GDG noted that the review did not consider evidence on the use of VLCD prior to bariatric surgery and believed this to be a separate issue. The GDG wanted to highlight that they did not want standalone VLCDs to be linked to the use of VLCD as a 2 week pre-surgery treatment. It was the opinion of the GDG that these diets should not be seen as a way to avoid surgery as although they do

	work for some people they are in general not as effective as bariatric surgery. The GDG were concerned that clinicians would use VLCDs routinely instead of bariatric surgery, and that the patient's treatment may be delayed as a consequence. The GDG also discussed the importance of highlighting that the use of VLCDs should not be considered as an alternative to surgery or a gateway to surgery. It was also noted that the definition of a VLCD diet has been amended since CG43 (see Glossary) which defined them as 1000 calories or less. This guideline has clarified and defined them as 800 calories or less, which is an accepted definition within current practice. The GDG selected adults and children over 2 years to be included within these VLCD reviews. However, no evidence was found for children for any of the VLCD reviews on effectiveness, safety or maintenance. VLCDs are not used on children in current practice and the GDG did not believe the evidence on adults could be extrapolated to make any recommendations on children. Similarly, it was not possible to make recommendations for any other of the identified subgroups or groups warranting special consideration. In line with advice from the co-opted expert for learning disabilities, the GDG noted that people with learning disabilities across the lifespan and carers supporting them should have access to specialist advice on overweight and obesity. They also felt that clinicians undertaking health checks for people with learning disabilities should be aware of referral pathways to services for individuals with obesity and thateducational programmes for health, education and social care staff should include training on assessing and managing overweight and obesity in people with learning disabilities.

8 Bariatric surgery in people with recent-onset type 2 diabetes

8.1 Introduction

Approximately 3 million people in the UK have type 2 diabetes (T2D); over a 500% rise since 1960. More than 100,000 people are diagnosed with the condition each year and it is likely that another million patients have yet to be discovered. Treatment already costs the NHS almost £10 billion a year which is 10% of its total budget.

The epidemic of obesity and T2D has been termed as "diabesity"; in most people the condition is managed with lifestyle advice and medication [41], but in some individuals with obesity, bariatric surgery has been used to aid weight loss. This often results in dramatic improvement in glycaemic control that may be partly independent of weight loss leading to the term 'metabolic surgery' as a descriptive term for the procedures used. In the most severely obese, it has been suggested that metabolic surgery may have the potential effect of putting diabetes into 'remission' in people who are obese. This is particularly pertinent as a potential 'treatment' option in those who have recent type 2 diabetes (within 10 years) as it may be possible to intervene before the impact of diabetes causes long-term damage to other organs.

The duration of T2D in adults who are obese is known to affect outcomes after surgery. Given the very high numbers of people with type 2 diabetes who are obese and the resulting health economic impact, the GDG wished to determine: "In people with recent-onset type 2 diabetes who are also overweight or obese, what is the clinical and cost effectiveness of bariatric surgery for the management of diabetes?"

8.1.1 Review question: In people with recent-onset type 2 diabetes (T2D) who are also overweight or obese, what is the clinical and cost effectiveness of bariatric surgery for the management of diabetes?

For full details see review protocol in Appendix C.

Table 36: PICO characteristics of review question

Population	Adults, young people and children with recent-onset type 2 diabetes (duration of less than or equal to 10 years) who are overweight or obese.
Intervention(s)	Bariatric surgery
Comparison(s)	Non-surgical management (including diet and exercise diabetes medication)
Outcomes	% weight loss (in BMI or kg) Use of diabetic medication Health related quality of life Remission of type 2 diabetes Improvement in glycaemic control Mortality Weight measured with BMI Weight measured in kg
Study design	RCTs or systematic reviews of RCTs

Studies that had less than 1 year follow-up were excluded as the long-term outcomes after bariatric surgery were considered the most important.

The definition of recent-onset diabetes of a duration of less than or equal to 10 years was determined by discussion with the GDG that indicated that 'remission' from diabetes following surgery was possible up to 10 years after an initial diabetes diagnosis.

8.1.2 Clinical evidence

We searched for randomised trials comparing the effectiveness of surgical interventions versus non-surgical management for people with recent-onset T2D and obesity. Recent-onset T2D was defined as within 10 years of diagnosis. Six studies[16,24,29,36,37,40,48,60,61] were included in the review; and are summarised in Table 37 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 39). See also the study selection flow chart in Appendix D, study evidence tables in Appendix G, forest plots in Appendix I, GRADE tables in Appendix O and excluded studies list in Appendix J.

Three studies[24,48,61] included people with a mean duration of T2D that was less than 10 years but with very large standard deviations which shows that there were a large proportion of patients who had T2D for longer than 10 years. These studies were considered to have indirect populations since they included a large proportion of people without recent-onset diabetes.

All outcomes were reported in at least 1 study. However, only 1 study[28,29,37,60,61] reported health-related quality of life after at least 1 year of follow-up. The study reported results from the RAND-36 questionnaire before and after treatment for each of the individual domains, but the study did not report composite scores across all domains. The study reports that there were significant improvements over conventional therapy in 5 of the 8 mental and physical domains among people treated with gastric bypass and 2 of the domains among people treated with sleeve gastrectomy.

The way diabetic medication usage was reported in the studies varied. Two studies [16,60] reported the proportion of participants who were still taking diabetic medication at follow-up (dichotomous) and 2 other studies[24,60] reported the number of diabetic medications being taken at follow-up (continuous). Consequently, both dichotomous and continuous outcomes were presented separately. Two of the other papers[36,40] reported this outcome in the surgery group only so it was not possible to include the results from these studies.

'Remission' of type 2 diabetes is often used as an outcome but there is controversy over the term as it is defined by hyperglycemia which may change over time[7]. The American Diabetes Association [7] has defined partial and complete remission. Complete remission is defined as a return to normal glycemic measures (HbA1C in the normal range, fasting glucose less than 100 mg/dl [5.6mmol/l]) of at least 1 year's duration in the absence of active pharmacological therapy or on-going procedures. Partial remission is sub-diabetic hyperglycemia (HbA1C not diagnostic of diabetes [less than 6.5%], fasting glucose 100-125 mg/dl [5.6-6.9 mmol/l]) of at least 1 year's duration in the absence of active pharmacologic therapy or on-going procedures.

Normal range of HbA1c is typically defined as less 6% [less than 43mmol/mol].
Remission of T2D was reported in a number of studies but the definition was different across the included studies. The different definitions are presented in Table 38.

As per the protocol, presentation of the results into the following 4 strata were explored: BMI 25-29.9 kg/m^2 at baseline, BMI 30-34.9 kg/m^2 at baseline, BMI 35-39.9 kg/m^2 at baseline, and BMI 40-49.9 kg/m^2. All of the studies included patients from more than one of these strata, but none of the studies performed subgroup analyses. Consequently, the results were separated by mean BMI and explored using sub-group analysis in the forest plots.

Table 37: Summary of studies included in the review

Study	Intervention/comparison	Population	Outcomes	Comments
Dixon 2008[16] Australia n=60 2 year follow-up	**Intervention:** Laparoscopic adjustable gastric banding with conventional diabetes care (n=30) **Comparison:** conventional diabetes care (with a focus on weight loss by life-style change) (n=30)	Obese patients (BMI >30 - <40 kg/m^2) with recently diagnosed (<2 years) type 2 diabetes Age: 20-60 years Mean BMI: 37.0 (SD 2.7) vs 37.2 (SD 2.5) kg/m^2 Mean HbA1C: 7.6 and 7.8% (60 and 62 mmol/mol)	% weight loss Use of diabetic medication (dichotomous) Remission of diabetes [a] Glycaemic control (HbA1C <6.2%) Mortality Weight in kg	Patients in the intervention group received all aspects of the conventional therapy program
Liang 2013[36] China n=108 1 year follow-up	**Intervention:** Laparoscopic Roux-en-Y gastric bypass (n=36) **Comparison:** usual conventional treatment plus Exenatide treatment (GLP-1 therapy) (n=36) or conventional treatment (medication, reduction in fat intake and physical exercise) (n=36)	Obese patients (BMI >28 kg/m^2) with type 2 diabetes (between 5 and 10 years) Age: 30-60 years Duration of T2D: 7.4 (SD 1.7) vs 7.2 (SD 1.8) vs 7.2 (SD 1.6) years Mean BMI: 30.5 (SD 0.9) vs 30.3 (SD 1.4) vs 30.3 (SD 2.0) kg/m^2 Mean HbA1C: 10.47 – 10.88% in arms (90.9-95.4 mmol/mol)	Remission of diabetes [a] Mortality Weight in BMI	Study conducted in China. In accordance with the WHO Asia-Pacific classification for obesity, BMI >28 kg/m^2
Mingrone 2012[40] Italy n=60 2 year follow-up	**Intervention:** patients assigned to undergo either gastric bypass (n=20) or biliopancreatic diversion (n=20) **Comparison:** conventional treatment (medication, programs for diet and lifestyle modification (i.e. reduction in fat intake and physical exercise)) (n=20)	Obese patients (BMI ≥35 kg/m^2) with type 2 diabetes (>5 years) Age: 30-60 years Duration of T2D: 6.0 (SD 1.2) vs 6.0 (SD 1.3) vs 6.1 (SD 1.2) years Mean BMI: 44.9 (SD5.1) vs 45.1 (SD 7.8) vs 45.6 (SD 6.2) kg/m^2 Mean HbA1C: 8.5 – 8.9% in arms (69.4 – 73.8 mmol/mol)	% weight loss Remission of diabetes [a] Mortality Weight in BMI Weight in kg	

Study	Intervention/comparison	Population	Outcomes	Comments
Palikhe 2013[48] India n=31 Mean 12.5 months follow-up	**Intervention:** laparoscopic sleeve gastrectomy (n=14) **Comparison:** intensive medical therapy with exenatide and low-calorie diet (1000 kcal/day) (n=17)	Patients with type 2 diabetes and BMI ≥ 27 kg/m^2 Age: 20 to 75 years Duration of T2D: 8.5 (SD 6.1) years Mean BMI: 40.5 (SD4.6) vs 35.8 (SD5) kg/m^2 Mean HbA1C: 8.5 and 8.7% (69.4-71.6 mmol/mol)	% weight loss Remission of diabetes[a] Glycaemic control (HbA1C <7%) Mortality Weight in BMI Weight in kg	Follow-up was mean 12.5 months; study is ongoing and only 20 patients had completed 12 months of follow-up
STAMPEDE trial (Schauer 2012/2014)[28,29,37,60,61] USA n=150 3 year follow-up	**Intervention:** patients assigned to undergo either gastric bypass (n=60) or sleeve gastrectomy (n=60) and intensive medical therapy **Comparison:** intensive medical therapy (n=60)	Obese patients with BMI 27-43 and type 2 diabetes Age: 20 to 60 years Duration of T2D: 8.2 (SD 5.5) vs 8.5% (SD 4.8) vs 8.9 (SD 5.8) years Mean BMI: 37.0 (SD 3.3) vs 36.2 (SD 3.9) vs 36.8 (SD 3.0) kg/m^2 Mean HbA1C: 9.0 – 9.5% in groups (74.9-80.3 mmol/mol)	% weight loss Use of diabetic medication (continuous and dichotomous) Remission of diabetes Health-related quality of life[a] Glycaemic control (HbA1C <6%, 6.5%, & 7%) Mortality Weight in kg	
The Diabetes Surgery Study 2013 (Ikramuddin 2013)[24] USA Taiwan n=120 1 year follow-up	**Intervention:** Roux-en-Y gastric bypass with lifestyle and medical management (n=60) **Comparison:** lifestyle and medical management only (n=60)	Patients with type 2 diabetes and BMI between 30.0 and 30.9 kg/m^2 Age: 30 to 67 years Duration of T2D: 8.9 (SD 6.1) vs 9.1 (SD 5.6) years Mean BMI: 34.9 (SD 3.0) vs 34.3 (SD 3.1) kg/m^2 Mean HbA1C: 9.6% (81.4 mmol/mol)	% weight loss Use of diabetic medication (continuous) Remission of diabetes Glycaemic control (HbA1C <6% and <7%) Mortality Weight in BMI Weight in kg	

(a) This is presented narratively only as composite scores were not available from the study

Table 38: Definition of remission of diabetes among included studies

Study	Remission definition
Dixon 2008	Fasting plasma glucose levels < 126 mg/dL HbA1c < 6.2% No oral hypoglycaemics or insulin.
Liang 2013	No definition given
Mingrone 2012	Fasting plasma glucose < 100 mg/dL (5.6 mmol per litre) Glycated haemoglobin < 6.5% for at least 1 year No active pharmacologic therapy.
Palikhe 2013	Fasting blood glucose < 100 mg/dl HbA1c < 6% on at least 2 occasions including the last follow-up visit No anti-diabetic medications
STAMPEDE 2014 (Schauer 2012/2014)	Glycated haemoglobin < 6% No anti-diabetic medications
The Diabetes Surgery Study 2013 (Ikramuddin 2013)	HbA1c < 7% LDL cholesterol level < 100 mg/dL Systolic blood pressure less than 130 mm Hg

Accepted definition: glycated haemoglobin (HbA_{1C}) less than 6% and fasting blood glucose less than 100 mg/dL off diabetic medications

Table 39: Clinical evidence summary: Surgical versus non–surgical management of people with T2D and obesity

Outcome	Number of studies	Imprecision	GRADE rating	Absolute Difference	Control event rate (per 1000)	Control event rate for continuous outcomes
% weight loss (BMI or kg)	5	No serious imprecision	Very low	20.54 lower (22.13 to 18.96 lower)	-	4.73%
Use of diabetic medication (dichotomous)	2	No serious imprecision	Moderate	16 fewer per 1000 (from 13 to 18 fewer)	25 per 1000	-
Use of diabetic medication (continuous)	2	No serious imprecision	Very low	MD 2.14 lower (2.48 to 1.80 lower)	-	Mean 2.6 medications used
Health-related quality of life	0[a]	-	-	-	-	-
Remission of type 2 diabetes	6	No serious imprecision	Very low	401 more per 1000 (from 234 to 663 lower)	64 per 1000	-
Improvement in glycaemic control (continuous)	5	No serious imprecision	Low	MD 1.32 lower (1.60 to 1.04 lower)	-	7.69% HbA1c
Mortality	6	No serious imprecision	Very low	N/A	0 per 1000	-
Weight measured with BMI (final score)	4	No serious imprecision	Low	MD 4.19 lower (4.62 to 3.76 lower)	-	Mean 31.8 kg/m^2
Weight measured in kg (final score)	5	No serious imprecision	Low	MD 19.48 lower ((22.61 24.2 to 16.36 lower)	-	Mean 104.8 kg

(a) One study did report quality of life but it did not report composite scores across all domains and it was not possible to analyse the results in the above table. There is a narrative summary in the clinical evidence section above

8.1.3 Economic evidence

8.1.3.1 Published literature

Four economic evaluations were identified with the relevant comparison and have been included in this review.[21,30,53,54] These are summarised in the economic evidence profiles below (Table 40 and Table 41) and the economic evidence tables in Appendix H.

Eight economic evaluations relating to this review question were identified but were excluded due to a combination of limited applicability, methodological limitations and the availability of more applicable evidence.[1,3,11,18,23,31,38,52] These are summarised in Appendix K, with reasons for exclusion given.

See also the economic article selection flow chart in Appendix E.

Table 40: Economic evidence profile: laparoscopic adjustable gastric banding (LAGB) versus conservative care for type-2 diabetes (T2D)

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
POLLOCK2013 [54] (UK)	Directly applicable[(a)]	Potentially serious limitations[(b)]	The economic evaluation was conducted using the CORE diabetes model. This model comprises of seventeen inter-dependent semi-Markov sub models each modelling a diabetes related complication. Patients with early onset type 2 diabetes and a baseline BMI of 37.1 kg/m^2 are modelled over a lifetime horizon. LAGB is compared to standard medical management comprising of normal diabetes care with a focus on weight loss through lifestyle change.	£3298	0.92 QALYs	£3602 per QALY gained	One way sensitivity analyses were conducted under 21 different scenarios. The ICER only increased above £20,000 to £36,377 in 1 scenario in which $HbA1_c$, SBP and BMI benefits were lowered to 1 standard deviation below the mean.
PICOT2012[53] (UK)	Directly applicable[(c)]	Potentially serious limitations[(d)]	The economic evaluation was conducted using a Markov model with a 20 year time horizon. The population was patients who have early onset type 2 diabetes and a BMI between 30 and 40 kg/m^2. LAGB is compared to a non-surgical weight loss program.	£1792	1.10 QALYs	£1634 per QALY gained	One way sensitivity analyses were run but results were not reported. The analysis was also run using a 2 and 5 year time horizon. At a £20,000 threshold LAGB was not cost effective at 2 years with an ICER of £20,159 but was cost effective at 5 years with an ICER of £4969. At a 2 year time horizon LAGB had an 11% probability of being cost effective at a £20,000 per QALY threshold. At a 20 year time horizon LAGB had a 100%

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
							probability of being cost effective at a £20,000 per QALY threshold.
KEATING2009 [30] (Australia)	Partially applicable[(e)]	Potentially serious limitations[(f)]	The economic evaluation was conducted using a Markov model with a lifetime horizon. The population was patients with early onset type 2 diabetes and a BMI between 30 and 40 kg/m^2. LAGB was compared to conventional therapy for the management of type 2 diabetes.	-£1088	1.20 QALYs	LAGB dominated conventional therapy	One way sensitivity analyses were conducted. LAGB remained dominant or cost effective in all but 1 scenario in which the relative risk of diabetes remission was reduced to the lower 95% CI and annual probability for relapse to type 2 diabetes increased to the upper bound of the 95% CI. Under this scenario the ICER increased to £21,449 per QALY gained.

Abbreviations: BMI: body mass index; HbA1c: glycated haemoglobin; LABG: Laparoscopic adjustable gastric band; SBP: systolic blood pressure

(a) UK cost utility study

(b) Study was funded by Allergan Ltd, the manufacturer of the LAP-BAND LAGB product. Unclear whether the model accounts for future weight regain. Mortality and loss of HRQoL from surgical complications are also not modelled

(c) UK cost utility study

(d) Does not look at mortality and loss of HRQoL associated with surgical complications. The study does not measure HRQoL using EQ-5D and a lack of long run clinical data has necessitated long-term extrapolation of clinical data based on assumptions

(e) Australian cost utility analysis

(f) *Study was funded by Allergan Ltd, the manufacturer of the LAP-BAND LAGB product. The study employs a basic model structure, which ignores obesity comorbidities other than T2D and mortality associated with surgery. Also the model does not take into account the effects of potential weight regain years after surgery*

Table 41: Economic evidence profile: gastric bypass versus standard care for T2D

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
HOERGER2010 (USA)	Partially applicable[a]	Potentially serious limitations[(b)]	The economic evaluation was conducted using the CDC-RTI Diabetes Cost-Effectiveness Model. This is a Markov model with a lifetime horizon that simulates diabetes-related complications. The population was patients with early onset diabetes and a BMI ≥ 35 kg/m^2. Gastric bypass is compared to standard care for type-2 diabetes.	£9884	2.21 QALYs	£4472 per QALY gained	A variety of one way sensitivity analyses were conducted. These included reducing the quality of life gain from a BMI reduction to zero. The ICER did not increase above £20,000 per QALY in any of the one way sensitivity analyses. At a £20,000 per QALY threshold gastric bypass had a 98% probability of being cost effective.

(a) US cost utility study

(b) Model does not explicitly account for weight regain; however there is a probability that the patient could relapse after diabetes remission. Although the study is based on the US healthcare system the costs detailed in the study, such as the cost of bypass surgery and post-surgical follow-up care, are far greater than UK costs. This means the study's results will bias away from the intervention. The study does not use EQ5D for HRQoL values

Unit costs

To further help the GDG consider the cost effectiveness of bariatric surgery the following costs for bariatric surgical procedures were identified using the NHS reference costs.[14]

Table 42: Bariatric surgery costs

Procedure	HRG code	Cost (£)[(a)]
Stomach Bypass Procedures for Obesity	FZ84Z	£5,410
Restrictive Stomach Procedures for Obesity	FZ85Z	£2,473

(a) Average total HRG costs

8.1.4 Evidence statements

8.1.4.1 Clinical

- Surgical intervention is more clinically effective than non-surgical management at:
  - Increasing percentage weight loss from baseline (5 studies, n=417; very low quality)
  - Reduction in use of diabetic medication (4 studies, n=306; moderate quality)
  - Increasing remission of diabetes (6 studies, n=503; very low quality)
  - Improving glycaemic control (5 studies, n=370; low quality)
  - Reducing weight as measured by BMI (4 studies, n=303; low quality) or kg (5 studies, n=398; low quality)
- These changes were considered to be clinically important differences.
- Mortality rates did not appear to differ between groups (6 studies, n=503; very low quality).
- One study reported improvement in quality of life across 5 domains in the gastric bypass procedure and 2 domains in the gastric sleeve procedure using a RAND 36 questionnaire.

8.1.4.2 Economic

- Two cost-utility analyses found that LAGB was cost effective compared to non-surgical management for treating obese patients with early onset type 2 diabetes (ICERs: £3602 per QALY gained, £1634 per QALY gained). These studies were assessed as directly applicable with potentially serious limitations.
- One cost-utility analysis found that LAGB was dominant (less costly and more effective) compared to non-surgical management for treating obesity in obese patients with early onset type 2 diabetes. This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-utility analysis found that gastric bypass was cost effective compared to non-surgical management for treating obese patients with early onset type 2 diabetes (ICER: £4472 per QALY gained). This study was assessed as partially applicable with potentially serious limitations.

8.1.5 Recommendations and link to evidence

Recommendations	**110. Offer an expedited assessment for bariatric surgery to people who with a BMI of 35 or over who have recent onset type 2 diabetes[v] as long as they are also receiving or will receive assessment in a tier 3 service (or equivalent).[new 2014]** **111. Consider an assessment for bariatric surgery in people with a BMI of 30-34.0 who have recent onset type 2 diabetes[o] as long as they are also receiving or will receive assessment in a tier 3 service (or equivalent).[new 2014]** **112. Consider an assessment for bariatric surgery in people of Asian family origin who have recent onset type 2 diabetes[o] at a lower BMI than other populations (see recommendation 36) as long as they are also receiving or will receive assessment in a tier 3 service (or equivalent).[new 2014]**
Relative values of different outcomes	The GDG considered the following outcomes to be critical to examine in the literature for this review: percentage weight loss, use of diabetic medication, and health-related quality of life at latest follow-up. The GDG also noted that the following were important outcomes: remission of type 2 diabetes, improvement in glycaemic control, mortality, and weight as measured in either BMI or kg (all at latest follow-up). The GDG felt that the most valuable way of measuring weight loss was one that took into account baseline values. Change values and final values of weight do not take into account the changes from baseline for each patient, so the GDG chose percentage weight loss (that is, the average of percentages of weight loss) as the most critical outcome to decision making when determining the effectiveness of bariatric surgery. However, as some studies do not report weight in this way, weight in BMI and kg were also included as important outcomes. The GDG felt that a reduction in diabetic medication was a crucial measure of how well bariatric surgery affected a patient's diabetic status as it assumes that the diabetes is well controlled so this outcome was examined in the literature. Other aspects of the patient experience after bariatric surgery were felt to impact greatly on the patient, so health-related quality of life was an outcome that the GDG found critical to decision making and so, examined in the literature. Although the GDG noted that the use of the term 'remission' of diabetes may be a misnomer since people are not 'cured' of diabetes, they did however think that this composite measure (as defined in the studies) is useful for determining the effect of bariatric surgery on diabetes. This outcome is typically defined as improvement in glycaemic control (≤6% HbA1c) and fasting blood glucose (less than 100 mg/dL), as well as no further need for diabetic medication. Acknowledging that some papers would not report the composite value of remission, but that an improvement in glycaemic control was a helpful measure on its own for the effect of bariatric surgery on remission, the GDG chose this as an important outcome to consider.

[v] The GDG considered that recent-onset type 2 diabetes would include those people whose diagnosis has been made within a 10 year time frame.

	While rare, the GDG were also interested in examining the difference in mortality rates between surgery and non-surgery within the literature.
Trade-off between clinical benefits and harms	Any intervention carries risk to the individual. Surgical intervention in overweight or obese people carries an increased risk of complications, for example, in relation to anaesthesia. However, this risk needs to be considered in terms of the potential benefits that can be achieved by surgically treating the condition of overweight or obesity, including creating a 'remission' of diabetes in this population and thereby avoiding long-term harm from that condition. People with T2D having surgery at different BMI thresholds may respond differently. For example, effectiveness may be less or greater in people with a higher or lower BMI. If evidence is available about effectiveness at different BMIs, the trade-off between benefits and harms may also differ.
Trade-off between net health benefits and resource use	Four economic studies were identified which evaluated the cost effectiveness of bariatric surgery in individuals with recent-onset T2D. Three studies looked at laparoscopic adjustable gastric bands (LAGB) compared to medical management of T2D. Of these studies, 2 found that LAGB was cost effective compared to non-surgical management for treating obese patients with recent-onset T2D (ICERs: £3602 per QALY gained and £1634 per QALY gained). Both of these studies used a UK NHS perspective and are therefore directly applicable to the UK NHS. One further study found that LAGB dominated (less costly and more effective) non-surgical management of T2D; however this was conducted using an Australian healthcare perspective and is therefore only partially applicable to a UK setting. The GDG agreed that, despite the limitations of these studies, the evidence to suggest that LAGB is cost effective in this population was convincing. Robust sensitivity analyses conducted within the studies supported this conclusion. One study looked at gastric bypass compared to standard medical management of T2D. The study showed that gastric bypass was cost effective at a £20,000 per QALY threshold, with an ICER of £4472 per QALY gained. However, the study was conducted using a US healthcare perspective and was therefore only partially applicable. The GDG noted that although the costs of surgery used in the model were much higher than UK surgery costs, the costs of diabetic care were also likely to be higher, meaning that the cost savings from reduced diabetic medication were also likely to be overestimated. Despite this, the GDG noted that addressing this limitation would not substantially change the model results as the sensitivity analyses revealed that the model was very robust to drastic changes in parameter values. Based on the existing evidence and consideration of the cost of surgery in the UK, the GDG agreed that bariatric surgery is highly likely to be cost effective for obese individuals with recent-onset T2D. The GDG noted that some individuals with a BMI between 30-35 kg/m^2 could achieve similar outcomes as those identified in the clinical review with a BMI over 35 kg/m^2. This was demonstrated in 1 study found in the clinical review. Such individuals may be identified through assessment as recommended above. One study identified in the economic literature search by Picot et al[53] found that bariatric surgery may be cost effective at a £20,000 per QALY threshold, for individuals with an 'identifiable obesity-related comorbid condition' and a BMI between 30 – 35 kg/m^2 (ICER: £13,701 per QALY gained). The authors note however that the result is based on weak evidence. Therefore for these individuals, bariatric surgery may also be a cost effective treatment but with less confidence in the evidence.
Quality of evidence	Overall, most of the evidence was of low or very low quality. Four of the outcomes were downgraded due to indirectness as the majority of the studies included a large proportion of people with diabetes for more than 10 years. While the GDG acknowledged that evidence on individuals with duration of T2D of 10 years or less

	would be ideal, they felt that the results from these studies were likely to reflect, if not underestimate, the results in people with more recent-onset diabetes. This was informed by the GDG experience of observational data from the latest National Bariatric Surgery Registry, which suggests that people with more established diabetes may be less likely to respond to bariatric surgery. There was also a high risk of bias in a large number of the included studies. This was due to a number of reasons including a risk of selection bias: only 1 study had adequate allocation concealment while none of the other studies reported on allocation concealment, 2 studies did not report about generation of randomisation sequence, and in a few studies, people in groups were up to 10 kg higher or lighter in the surgery groups. Furthermore, there was also a lack of blinding, which, while it is not easily possible for the treatments, can still affect more subjective outcomes. Some studies had either differential dropout rates or no information reported about dropout rates. Some outcomes were imprecise and this was largely due to small sample sizes in some of the included studies. The body of evidence considered, which was based on 6 studies, showed that bariatric surgery consistently improved weight and diabetic outcomes compared to non-surgery in people with recent onset T2D (less than 10 years). Most of the evidence considered included people who had diabetes for less than 10 years, but some studies also included individuals who had diabetes for more than 10 years. It was not possible to assess differential mortality since no deaths were reported for either surgery or non-surgery in any of the included studies. Quality of life was reported in 1 study[60] from the RAND-36 questionnaire but was only presented narratively because results were reported for each domain, rather than as a composite outcome. As specified in the protocol, evidence was presented separately by mean BMI. However, with few studies for many strata, it was difficult to comment about differential effect on different BMIs. Two studies had a mean BMI from 30 to 34.9 kg/m^2 (though only 1 reported many of the outcomes of interest), 3 had mean BMI 35-39.9 kg/m^2, but only 1 study had mean BMI between 40 and 49.9 kg/m^2. While some studies included some people with a BMI of less than 30 kg/m^2, there were no studies where the mean BMI was less than 30 kg/m^2. Areas where it was thought that the results might differ (and to examine if there was heterogeneity in the results) included gender, diabetes treatment (particularly use of insulin), ethnicity, use of VLCD, exercise (supervised or advice only), and type of surgery. However, the heterogeneity in all but 1 of the analyses was not important since all studies showed significant benefits for the surgery arm. Many of the studies did not report the ethnicity of the participants or present the results separately by ethnicity. While there were a few studies in Asian countries which included participants at lower BMIs (1 in India, 1 in China and 1 with centres in both the US and Taiwan), the GDG did not feel they could draw conclusions from the evidence considered about the appropriateness of different BMI thresholds for surgery in these individuals.
Other considerations	The GDG felt that the evidence supported and strengthened the existing recommendation from CG43 for people with T2D and a BMI of 35 or above being offered surgery. They chose to remove the original reference to diabetes from within the existing recommendation relating to surgery in CG43 and made a separate recommendation for the population of obese (BMI 35kg/m^2 or over) people with recent-onset diabetes, reflecting the evidence considered in this review.

There was only 1 study with a mean BMI of 30-35 kg/m^2, and the GDG felt that this was not sufficient to support the routine referral for assessment for bariatric surgery in this population. The GDG felt that referral for assessment for bariatric surgery in this group should only be considered in exceptional circumstances (for example, people with other obesity related issues or where diabetes is not being sufficiently managed with alternative measures such as diet, exercise and pharmacological treatments). Given that bariatric surgery may be of some benefit to some individuals, the GDG considered that it was important that healthcare professionals at least considered offering an assessment for individual patients with BMI less than 35 kg/m^2 on a case-by-case basis, and made a weaker recommendation in this regard reflecting the evidence considered.

While there was limited data on quality of life reported in the included studies, the GDG felt, from their experience, that the improvement in quality of life from treating diabetes would outweigh possible harms from bariatric surgery. The GDG highlighted the importance of collecting data on quality of life in this population in the future. The GDG felt that, from a patient perspective, an improvement of quality of life following surgery would be significant. The GDG noted that there were additional effects of conducting bariatric surgery on other obesity related conditions (for example, joint pain or stress incontinence), as well as diabetes, which can have a significant impact upon an individual's quality of life.

The GDG noted that diabetes tends to occur at lower BMIs in Asian patient due to greater abdominal adiposity. The GDG felt that it might be appropriate to consider bariatric surgery at lower thresholds in these individuals. The GDG did not consider that it was possible to specify an exact BMI threshold for this population, but noted that the International Diabetes Federation recommends that for people of Asian origin, BMI thresholds for eligibility and prioritisation of bariatric surgery should be reduced by 2.5 BMI points[15]. They made a consensus recommendation in the absence of any evidence in this review in ethnic minorities recognising the established evidence elsewhere for this group. The GDG noted that NICE public health guidance (PH46 BMI and waist circumference - black, Asian and minority ethnic groups) had identified that these groups are at an equivalent risk of diabetes, other health conditions or mortality at a lower BMI than the white European population. It also noted that the guidance had not found sufficient evidence to make recommendations on the use of new BMI and waist circumference thresholds to classify whether members of these groups are overweight or obese.

The GDG also noted that while most studies included both male and female patients, the results were not reported separately by gender so it was not possible to comment about any differences of bariatric surgery by gender. The GDG considered that women are more likely to have a BMI of over 40 and more likely to access services and felt that it was important that men were encouraged to access services so that they also have opportunities to benefit from effective treatments. They did not wish to make a recommendation in this area.

The GDG acknowledged that different procedures may have different effectiveness and safety profiles, but the limited evidence prevented the GDG from making any specific comment about differential effect of different procedures. Evidence on biliopancreatic diversion was reported in 1 study and included in the review despite the fact that it is only very rarely used in the UK. The results tend to be slightly better than other types of surgery as it is the most invasive surgery used, but there are concerns about the safety of the procedure and people who receive this procedure usually require life-long follow-up. However, the results from this study were removed from the outcome 'improvement in glycaemic control' as it was felt that

the results were skewed because of this study. The study reported $HbA1_c$ levels less than 5% in the group that received this treatment; the GDG felt that it was very unlikely that $HbA1_c$ would be this low for any other type of surgery.

With regards to the other factors which may have differentially affected the results presented in this review (see Appendix C), the GDG noted that most were not reported adequately enough in the studies to consider, and would have been limited by the small number of included studies. These included the use of a VLCD, concomitant supervised exercise versus advice on exercise only, and the use of insulin. Most studies included a mix of participants who did and who did not use insulin, but studies did not report the results separately for these individuals. However, the GDG felt, from their clinical experience, that it was likely that people with insulin resistance were more likely to benefit from bariatric surgery and that people who have poor beta cell function are less likely to benefit. Consequently, it may be important to consider measuring c-peptide as an index of beta-cell function in individuals who are being considered for surgery.

The GDG also wished to highlight that bariatric surgery does not result in the cure of diabetes, despite how this is often referred to in the literature. The term 'remission' has been used throughout the document to reflect the terminology used in the studies, despite the fact that the definition often varied slightly among the included studies. The GDG were aware that this concept is often misunderstood by patients and that a perception that diabetes has been cured can mean that some people choose not to continue to access services that are appropriate and important for their health.

The GDG debated the timing of bariatric surgery, noting from the evidence that having surgery within 3 years of the onset of diabetes could avoid complications but that the long-term impact on microvascular disease remains unknown. They discussed the fact that the chances of getting any individual into a bariatric pathway within a 2 year diagnosis of T2D with current commissioning guidelines is very challenging. However, the group felt that surgery within 10 years of diabetes onset could also reduce or delay the need for diabetic medication. The GDG noted that this reduction in medication may be temporary because, as the disease progresses, there is often a need to reintroduce medications. They agreed however that surgery was still worthwhile in this group as there was improved glycaemic control and reduction in medication usage. For these reasons, the GDG did not wish to indicate a specific time frame in their recommendations.

Furthermore, in relation to the timing for surgery, the GDG wanted to highlight that while the existing recommendation 92 from CG43 recommended a number of criteria that patients must fulfil before bariatric surgery is considered a treatment option, including that all appropriate non-surgical measures must have been tried. The GDG noted that this should not be a specific criterion that has to be fulfilled before referral for assessment for bariatric surgery in patients with type 2 diabetes as it could create unnecessary delays. The GDG felt that individuals with type 2 diabetes and a BMI of 35 or over should have an expedited referral for assessment for bariatric surgery, ideally from within a tier 3 service. The GDG were aware that further guidance on tier 3 Obesity services can be found in the NHS England report on Joined up clinical pathways for obesity.

They recognised the artificiality of the 'tiers' as currently defined especially the challenges in universally commissioning these services. here tier 3 services are not currently commissioned or available then the GDG felt that, in order to facilitate their timely pathway through for bariatric surgery as considered appropriate, individuals must be supported and evaluated in the short term by equivalent services

	until tier 3 services are available. For this reason, they added further clarification to their recommendations to allow appropriate referrals from other services which they defined as equivalent. For example, the GDG felt that medical assessment could take place within a tier 4 service if properly configured with a full multidisciplinary team including a physician. The GDG noted that for patients the referral to a tier 3 service, including for consideration for bariatric surgery, is often seen as a failure on their part. The GDG felt it was important to emphasise to people that this is not the case, but that it represents another treatment option that may be appropriate for the individual. The GDG highlighted that it was also important for healthcare professionals to optimise HbA1c levels prior to any surgery but did not feel that this required a recommendation as it was considered current practice, as per the British Obesity and Metabolic Surgery Society Tier 3 commissioning guidance. The GDG chose not to amend the recommendation on bariatric surgery in children and young people with type 2 diabetes as no evidence was identified. The GDG were aware from expert opinion that there remained challenges in relation to people with learning disabilities accessing services. They felt it was important that people with learning disabilities do have access to specialist advice and that clinicians undertaking health checks for people with learning disabilities should be aware of referral pathways to services for individuals with obesity. They recognised that surgery in this group was rarely considered as an option because of the difficulties with gaining informed consent and because there may be challenges with compliance to advice following surgery. They did note, however, that educational programmes for health, education and social care staff should include training on assessing and managing overweight and obesity in people with learning disabilities. The GDG considered the cost implications from increasing access to assessments for bariatric surgery. Looking at the economic evaluations presented in the economic evidence the GDG noted the considerable cost-savings derived from reduced diabetic and obesity related co-morbidities. Once these future costs have been deducted the overall cost of bariatric surgery to the NHS is small relative to the large, clinically proven, gains the individual receives. The GDG also noted that a considerable number of individuals may choose not to be referred for assessment. There may be people in these circumstances who are referred for assessment for bariatric surgery and are not suitable or choose not to have it.

9 Follow-up care packages

9.1 Introduction

A post- bariatric surgery care package is ideally provided by a multidisciplinary team (MDT) offering a multicomponent approach, with some variation in local models of care. It is believed that multidisciplinary evaluation is vital to providing best patient care and in current NHS arrangements, the follow-up team may include bariatric physicians, dietitians, practitioner psychologists or psychiatrists, specialised nursing staff, physiotherapists or exercise specialists, and surgeons. The individual's general practitioner (GP) may be involved in requesting annual blood tests or review appointments via a local shared care weight gain agreement. All practitioners recognise that after all procedures there is a minimum level of life-long follow up needed to support good clinical care with variation depending on the type of surgery and individual needs of the patient.

Current practice is that initial outpatient follow up should be offered by the tier 4 surgical team to all individuals at 4-6 weeks post-surgery. The surgical aftercare period in the current Commissioning Policy A05[57] is 2 years at the surgical centre with recommended life-long nutritional follow up by tier 3 or 4 services. Individuals need long-term follow up as nutritional and vitamin deficiencies occur at a significant rate,[39] requiring micro-nutrient monitoring and access to specialist services as needed. The extended period of surgical aftercare is generally considered important to optimise outcomes, supervise long-term nutritional and dietary replacement and to identify issues that may require referral back to the medical and surgical MDTs. This may include treatment of comorbidities, investigation and treatment of medical and surgical complications (for example, hypoglycaemia, dumping syndrome), and where there are clear surgical or medical indications, addressing weight regain. Ideally, bariatric physicians and surgeons should liaise closely with local tier 3 services and GPs after surgery and consider a shared care model of chronic disease management that arranges for each patient to be reviewed (including nutritional screening) at least annually, indefinitely, with clear protocols for the management of different complications and nutritional deficiencies if they arise.[57]

Reasons for long-term follow up were reviewed by the National Confidential Enquiry into Peri-operative Death after bariatric surgery.[42] This report emphasised the importance of offering the full range of multidisciplinary input pre- and post-surgery and supporting the individual's needs including improving access to psychological assessment, screening, dietetic education and support. Clear contact details for referral back into the specialist weight management service are required for specialist treatment for example in the event of pregnancy or where plastic surgery is indicated.[6]

The current professional standards in the UK include a commitment to long-term follow up with appropriate level of surgical, dietetic, psychology or psychiatric, medical and nursing input. The latest commissioning guidance mandated long-term data collection of patients' outcomes with local and national audit results which should be publically available. The challenge in the NHS currently is ensuring that people who have had bariatric surgery have access to such long-term follow-up. Where local tier 3 services do not exist, the provision of what might be considered standard follow-up post-bariatric surgery is variable. Given the importance of minimising harm from unidentified micronutrient deficiencies, suggested improvements in access to psychological follow-up and the importance of maximising outcomes, the GDG wished to identify which components of a follow-up care package optimised patient outcomes.[42]

9.1.1 Review question: What is the clinical and cost effectiveness of follow-up care packages after bariatric surgery compared with usual care?

For full details see review protocol in Appendix C.

Table 43: PICO characteristics of review question

Population	Adults (18 years and older) and young people (post-puberty) who are overweight or obese and who have undergone bariatric surgery
Intervention(s)	Follow-up care package after bariatric surgery that includes nutritional monitoring and 1 of the following: - problems associated with excess weight loss - avoiding weight regain - specialist psychological, educational, and social support Note: support for becoming pregnant post-bariatric surgery may also be part of the care package
Comparison(s)	Usual care (defined as nutritional monitoring only – not a package; nutritional monitoring includes assessment of dietary history, weight measurements, blood tests, and face-to-face review)
Outcomes	Critical: 1. % weight loss at latest follow-up (in BMI or kg) (or % excess weight loss) 2. Development of at least 1 micronutrient deficiency (i.e. iron, selenium, zinc, vitamin A, calcium, vitamin B12, vitamin B1) at latest follow-up 3. Health related quality of life / Obesity related quality of life at latest follow-up Important: 4. Reoperation rate at latest follow-up 5. Mortality at latest follow-up 6. Reduction in medication use at latest follow-up 7. Psychological well-being at latest follow-up
Study design	RCTs or systematic reviews of RCTs (conference abstracts if no evidence)

People with learning difficulties may be at a higher risk of complications and require additional follow up or support and may be at greater risk of continued excess food intake despite having the procedure. This group may also be at greater risk of nutritional deficiencies. Any evidence on people with learning disabilities would be presented separately, as the evidence allows.

In addition, it was felt that an absolute minimum study duration of 1 year was required for study inclusion since less than 1 year of follow-up would provide insufficient information on patients after bariatric surgery that require long-term follow-up.

The search was conducted from 2006 onwards as it was felt that care after bariatric surgery before this date was unlikely to be applicable to current practice.

9.1.2 Clinical evidence

We searched for randomised trials looking at the use of follow-up care packages after bariatric surgery. We considered those which compared usual care, defined as nutritional monitoring only, with follow-up care packages including nutritional monitoring and 1 or more additional component that was aimed at avoiding problems associated with excess weight loss, avoiding weight regain, or providing specialist psychological, educational and social support.

Two studies were included in the review[26,49] and are summarised in Table 44below.

One study[49] was on a very specific population of severely obese women (greater than 40 kg/m^2) after undergoing vertical banded gastroplasty (VBG), which is not currently used in the UK. This study considered a lifestyle intervention compared with usual care. Usual care consisted of 30 sessions over 3 years with a dietitian aimed at giving general information on adopting healthier eating and increasing physical activity (this is more comprehensive than current UK care). The lifestyle intervention consisted of an additional 40 minutes of individualised sessions during their 30 visits with the dietitian. The intervention aimed to help people overcome barriers and regulate their body

weight, adopt healthier eating habits and become less sedentary, using a patient-centred collaborative approach and behaviour modification techniques.

The other study[26] recruited participants that had undergone bariatric surgery 3 or more years previously and had lost less than 50% excess weight. The comparator in this study was wait list control. No additional information was given about what this included. However, the GDG agreed it was acceptable to assume that they had received some element of nutritional monitoring as this was usual care. Outcomes were measured at 12 months.

Evidence from these studies are summarised in the clinical evidence summary below (Table 45). Of the outcomes specified in the protocol, the included studies only reported percentage excess weight loss. As the studies did not report any of the other outcomes in the protocol, actual weight in kg at the end of the study was also reported. Outcomes 1 year after surgery were expected to be different from outcomes 3 years after surgery so it was felt inappropriate to pool results from these studies and they are presented separately.

See also the study selection flow chart in Appendix D, study evidence tables in Appendix G, forest plots in Appendix I, GRADE tables in Appendix O and excluded studies list in Appendix J.

Table 44: Summary of studies included in the review

Study	Intervention/ comparison	Population	Outcomes	Comments
Kalarchian 2012[26] US	Behavioural programme to help weight loss with dietary and physical activity delivered in groups and with telephone support versus wait list control group	n=36 patients with a BMI of 30 or more who had undergone bariatric surgery at least 3 years before and had less than 50% excess weight loss	Percentage weight loss at 12 months, change in weight in kg at 12 months	Dropouts: 5 in intervention and 2 in control arm Any treatment received by the wait list control group was not described
Papalazarou 2010[49] Greece	Usual care plus additional behavioural support focusing on nutrition education, dietary intake, and physical activity delivered by dietitian versus usual care (dietary advice and nutritional monitoring only) (both over 3 years)	n=30 severely obese women (BMI > 40 kg/m^2) who underwent vertical banded gastroplasty	Percentage weight loss at 3 years, weight in kg at 3 years	Study does not report how many participants were randomised to each arm; it is assumed that it is 15 per arm

Table 45: Clinical evidence summary: Usual care (nutritional monitoring only) versus usual care plus specialist educational support, and avoiding weight regain

Outcome	Number of studies	Imprecision	GRADE rating	Absolute Difference	Control event rate (per 1000)	Control event rate for continuous outcomes
% weight loss (excess) at 3 years	1	Serious	Very low	MD 26% higher (15.26 to 36.74% higher)	n/a	49.1%
% weight loss (excess) at 1 year	1	No serious imprecision	Low	MD 4.9% higher (2.43 to 7.37% higher)	n/a	0.9%
Weight loss at 3 years	1	Serious	Very low	MD 18.30 kg higher (from 27.73 to 8.87% lower)	n/a	102.5 kg
Mean change in weight loss at 1 year	1	Serious	Very low	MD 3 kg higher (from 9.17 lower to 3.17% higher)	n/a	-0.6 kg
Development of at least 1 micronutrient deficiency (iron, selenium, zinc, vitamin A, calcium, vitamin B12, vitamin B1)	0	-	-	-	-	-
Health related quality of life	0	-	-	-	-	-

9.1.3 Economic evidence

9.1.3.1 Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

9.1.3.2 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Nutritional monitoring (standard care)

Nutritional monitoring has 3 components: follow-up visits, nutritional supplementation, and blood tests. The costs of these components are detailed in the following sections. The costs below represent the majority of costs that are likely to be incurred; however regional costs may vary.

Follow-up visits

The costs associated with follow-up visits are displayed in Table 46. For the initial 2 years after surgery these visits are likely to take place with a dietitian or bariatric physician. It is assumed that in the first year the person has 3 visits, then in subsequent years the individual has 1 follow-up visit per year. After the initial 2 years, follow-up is likely to take place with either a dietitian, or with the GP within a locally agreed shared care protocol. These annual visits will take place for the remainder of the individual's life.

Table 46: Cost of follow-up visits

Health care professional	Number of annual visits	Length of visit (minutes)	Cost per visit	Source
First year post-surgery				
Dietitian	3	20 minutes	£31	PSSRU[12]
Second year post-surgery				
Surgical consultant	1	20 minutes	£33	PSSRU[12]
Subsequent years				
Dietitian[(a)]	1	15 – 60 minutes	£8 - £31	PSSRU[12]

(a) In some cases this appointment may take place with a GP

Nutritional supplements

Table 47 shows the costs of the nutritional supplements a patient may take during follow up. Note that some individuals may require additional nutritional supplements and individuals who receive a gastric band or a sleeve gastrectomy may not require these supplements. The exact nutritional supplements provided will be individualised to meet the person's requirements; the following costs represent an average.

Table 47: Cost of nutritional supplements

Supplement	Frequency	Cost per dose	Cost per year	Source
Ferrous sulfate (Tablets, coated, dried ferrous sulfate 200 mg (65 mg iron))	Once daily	£0.04	£14	NHS drug tariff[45]
Folic acid (Tablets, 400 mcg)	Once daily	£0.03	£11	NHS drug tariff[45]
Vitamin B12 injection (hydroxocobalamin)	Once every 12 weeks	£3.92	£17 (a)	PSSRU[12] & NHS drug tariff[45]
Multivitamin and mineral (Forceval)	Once daily	£0.16	£58	BNF[25]
Adcal-D3 Colecalciferol 400unit / Calcium carbonate 1.5g chewable tablets	Once daily	£0.07	£24	NHS drug tariff[45]
	Total		£124	

(a) Cost per injection includes 5 minutes of GP practice nurse time[12] and cost of injection (£1)[45]

Blood tests

To monitor potential deficiencies after bariatric surgery, people will require a blood test before their follow-up visit so that results can be discussed during the appointment. Examples of blood tests used are full blood count (FBC) tests, and liver function tests (LFTs), which would both be performed 3 times in the first year post-surgery and then once annually. Different tests are required depending on the type of bariatric surgery which has been carried out; therefore the annual cost of blood tests will also depend on the type of bariatric surgery. The GDG estimated that the annual cost of conducting: full blood count (FBC), urea and electrolytes (U and Es), liver function tests (LFTs), bone tests (calcium and parathormone), vitamin D, iron studies, B12, folate, fasting lipids and $HbA1_c$ would be £178 including 5 minutes of physician time to review the results. The total annual costs of nutritional monitoring are summarised in Table 48.

Table 48: Total cost for minimal follow-up

Years after surgery	Visits	Supplements	Blood tests	Total
1	£31	£124	£178	£333
2	£33	£124	£178	£335
3 onwards (with dietitian)	£8 - £31	£124	£178	£310 - 333

Economic considerations

Using the incremental cost of providing 2 years of follow up, relative to nothing, the QALY increase which would be required for 2 years of follow-up to be considered cost effective at a £20,000 per QALY threshold can be calculated like so:

$$Change\ in\ QALYs = \frac{Change\ in\ cost}{£20{,}000}$$

Therefore if 2 years of follow-up post-surgery costs £668 then it will need to produce 0.0334 QALYs to be considered cost effective at a £20,000 per QALY threshold.

9.2 Evidence statements

9.2.1 Clinical

9.2.1.1 Immediately post-surgery:

- Evidence from 1 RCT of 29 participants showed that a post-bariatric follow-up care package may have a clinical difference over usual care in terms of % excess weight loss after 12 months (low quality).

9.2.1.2 At least 3 years post-surgery:

- Evidence from 1 RCT of 30 participants showed that a post-bariatric follow-up care package may have a clinical benefit over usual care alone in terms of % excess weight loss after 3 years (very low quality).

9.2.2 Economic

- No relevant economic evaluations were identified.
- An original comparative cost analysis showed that:
  - Two years of post-bariatric follow-up would need to produce 0.0337 QALYs to be considered cost effective at a £20,000 threshold.
  - This analysis was considered directly applicable with potentially serious limitations.

9.2.3 Recommendations and link to evidence

Recommendations	**112. Offer people who have had bariatric surgery a follow-up care package for a minimum of 2 years within the bariatric service. This should include:** • **monitoring nutritional intake (including protein and vitamins) and mineral deficiencies** • **monitoring for comorbidities** • **medication review** • **dietary and nutritional assessment, advice and support** • **physical activity advice and support** • **psychological support tailored to the individual** • **information about professionally-led or peer-support groups.[new 2014]** **114. After discharge from bariatric surgery service follow-up, ensure that all people are offered at least annual monitoring of nutritional status and appropriate supplementation according to need following bariatric surgery, as part of a shared care model of chronic disease management.[new 2014]**
Relative values of different outcomes	The GDG considered the following outcomes to be critical to examine in the literature for this review: Percentage weight loss at latest follow-up, development of at least 1 micronutrient deficiency at latest follow-up, and health-related quality of life at latest follow-up. The GDG also noted that the following were important outcomes: re-operation rate, mortality, reduction in medication use and psychological well-being (all at latest follow-up). The GDG felt that the most valuable way of measuring weight loss was one that took into account baseline values. Change values and final values of weight do not take into account the changes from baseline for each patient, so the GDG chose percentage weight loss (that is the average of percentages of weight loss) as the most critical outcome to decision making when determining the adequacy of follow-up care packages. However, as one study did not report any other outcomes specified in the protocol, final weight scores were also reported. The GDG were concerned with people not receiving an adequate diet after bariatric surgery, so felt that micronutrient deficiency was another critical outcome in their decision-making which they wished to examine in the evidence. Other aspects of the patient experience after bariatric surgery were felt to impact greatly on the individual so health-related quality of life was an outcome the GDG found to be critical to decision making. Reoperation rates were thought to be a particularly important measure of the adequacy of a care package after bariatric surgery. While rare, the GDG were interested in examining the difference in mortality rates between different care packages after bariatric surgery within the literature. The GDG found the requirement for medication (particularly for comorbidities such as diabetes or hypertension) in the follow-up period after bariatric surgery to be a useful outcome when comparing a care package with usual care.

	Although this was considered to be part of health-related quality of life, the GDG felt that the psychological well-being of people after bariatric surgery is particularly important, so any evidence of differences in psychological well-being resulting from different care packages was considered.
Trade-off between clinical benefits and harms	One study (Papalazarou 2010[49]) found post-bariatric care packages to be more clinically effective than usual care at increasing % weight loss. However, the GDG interpreted this evidence of benefit with caution for a number of reasons. Usual care in this study (Papalazarou 2010[49]) was not representative of usual care in the UK. The GDG considered it to be above the level of care given in the UK with extensive follow-up appointments. The GDG also discussed the fact that the higher baseline weight in the intervention arm (4-5 kg based on a difference of 1.5 kg/m^2 BMI) could have influenced the outcome. They also felt mistrustful of the data given the lack of information on withdrawals and the small study size. After bariatric surgery, there is likely to be at least some withdrawals, particularly in those people with poorer outcomes and over 3 years of follow-up. Given the uncertainty in the number of participants included in the final outcomes reported, there was very little confidence in the results. Another study[26] compared post-bariatric care packages to usual care in people that had undergone bariatric surgery 3 or more years prior to the study and had less than 50% excess weight loss. Post-bariatric care packages were found to be more clinically effective than usual care at 12 months follow-up. However, the GDG felt that people who have had bariatric surgery have particular needs. They felt that current practice in the UK was not consistent and, in their experience, people are often lost to follow-up after bariatric surgery. From their experience, the GDG felt that an active level of follow-up care was necessary in order to give people support with different aspects of the patient experience (see 'Other considerations' below). The GDG did not consider there to be any harms associated with the provision of a follow-up package of care but recognised the very real harm to the individual if nutritional deficiencies were not appropriately identified or managed in a timely manner.
Trade-off between net health benefits and resource use	No economic evaluations were identified in the literature. It was estimated that providing the minimal level of care would cost approximately £668 for the first two years post-surgery. At this cost, follow-up care would need to produce 0.0334 QALYs to be considered cost effective at a £20,000 per QALY threshold. The GDG recognised that the consequences of not providing this level of care can be severe: high probability of weight regain, depression, nutritional deficiencies, osteoporosis, anaemia, and even death. There would also be significant costs involved in treating these outcomes. Therefore the GDG agreed that follow-up as specified is highly likely to be cost effective at a £20,000 per QALY threshold, as not only will it provide significant health improvements, but it will also reduce future NHS costs.
Quality of evidence	Two studies[26,49] were included in the clinical review. One study[49] reported on a small and very specific population of 30 severely obese women who had undergone vertical banded gastroplasty, a procedure not currently used in the UK. Of the outcomes of interest to the GDG (and specified in the review protocol), the study only reported percentage excess weight loss at end of study. No information was given in the study about how many participants were in each

	arm of the trial, so it was assumed that it was a 50-50 divide. No information was given on study withdrawals, a common problem in post-bariatric care, particularly for people with poor outcomes. As a result, the results are likely to overestimate the effectiveness of the intervention. Overall, the study was found to be at very high risk of bias. There were no details of the randomisation sequence or if there was allocation concealment (selection bias), no details on how the outcome was calculated (measurement bias), issues related to lack of blinding, and, as described above, there were no details of dropouts so there is a high risk of incomplete outcome bias. The other study[26] was a small and selective population comprised of people who had bariatric surgery 3 or more years previously and had less than 50% excess weight loss. Usual care was defined as a wait list control without any further information given. The GDG felt that it was acceptable to assume that this included nutritional monitoring. Both studies reported 1 critical outcome (% excess weight loss) which was very low quality. The GDG agreed that the evidence for this question was limited and of poor-quality, and made consensus recommendations based on their experience and opinion. No relevant evidence was available for consideration from the conference abstracts identified in the search for this review question. No evidence was found to inform recommendations in the pre-specified subgroups or strata in the protocol including for young people (from post-puberty to 18 year), by surgery type, for different ethnicities, for people with T2D, or for people with learning disabilities.
Other considerations	The GDG considered the applicability of these studies and discussed the challenges in providing care in this area. Current practice is variable and the GDG felt that, while research into different care packages for a longer period of follow up would be valuable, it was important to provide advice for the NHS now to mitigate against poor care and to encourage long-term sustainable positive outcomes. Consequently, the GDG chose to make a number of consensus recommendations. The GDG noted the limited poor-quality evidence and therefore the recommendations were drafted based on the experience and opinion of the GDG. The GDG felt that their draft recommendations were applicable to adults and children, and that the detail contained within them could apply to those population sub-groups where they had looked for evidence but did not find any (for example, people with learning disabilities or individuals from different ethnic minorities). For the purposes of this review, the GDG chose nutritional monitoring as a comparator as this is assumed to be the very minimum level of care that should be provided post-bariatric surgery (although current practice is variable in terms of quality). The GDG felt that a number of areas would be important to consider as part of a follow-up care package to ensure safety and wellbeing after bariatric surgery. These included specific interventions and also a clarification of a time frame regarding the follow-up. **Within the bariatric service** The GDG noted that the nature and quality of follow-up care varied around the UK. The GDG were unanimous that that follow-up care needs to be provided by the

surgical team (tier 4) for a minimum of 2 years in the first instance. They noted that this 2 year time frame was also in line with the Tier Commissioning Guidance recommendations.[57]They made a strong recommendation about this on the basis that it would be unethical not to offer this follow-up care.

As well as specifying that nutritional status should be monitored at least annually after discharge from a bariatric surgery service for all patients with no time limit, the GDG chose also to include this in a package of follow-up care to allow screening for and replacement of nutritional, vitamin and mineral deficiencies to sit alongside appropriate dietetic assessment, advice and support after surgery. Furthermore, the GDG felt that, from their experience, up to a third[27] of people having bariatric surgery would have good weight loss initially but then experience weight regain. Consequently, they felt that provision of appropriate dietary advice and support with behavioural change and access to tailored psychological and wellbeing assessment, advice, and support as required should also be available in order to mitigate against this wherever possible.

The GDG noted the importance of monitoring comorbidities such as T2D, since some individuals may ultimately have relapse of diabetic symptoms (for example, a lack of glycaemic control) after initial improvements following surgery. The GDG highlighted the need to continue screening for retinopathy in these individuals, given the potential risk of missing sight-threatening problems.

The GDG also noted that many people who have had bariatric surgery have not previously been in a position to exercise because the degree of their obesity limited physical activity. The GDG felt that providing specialist physical activity and support would be an important component of any follow-up care package, and that this should be tailored to the person to ensure that any barriers to exercise or increased physical activity after surgery were removed (for example, lack of knowledge or understanding of the benefits of exercise).

The group discussed the importance of providing access to psychological screening and support following surgery and were aware that the need for and the degree of psychological intervention required would vary between individuals and over time. CG43 made recommendations regarding pre-operative psychological support including the availability for such support after surgery by a multidisciplinary team (original recommendation 1.2.6.9 adults and 1.2.6.14 children). Psychological needs after bariatric surgery can vary enormously and can include issues such as adjusting to changes in the relationship with food and body size, managing the impact on social relationships, as well as dealing with excess skin including consequent difficulties with hygiene, activity and self-image. The patient members of the group identified clearly with the challenges that this may bring, reporting that a number of people may require 'body-contouring' plastic surgery to remove excess skin in order to maximise opportunities for physical activity, sexual function and psychological health.

The GDG discussed the issue of the provision of follow-up social support, and noted the value that social support, both professionally led and local peer support groups (including online and local groups) can offer in aiding the delivery of some of the elements of a follow-up care package and in helping to maintain weight loss. It was particularly noted that people can discharge themselves from services following surgery as all seems to be going well and they have lost the weight intended through surgical measures. It was noted that a follow-up care package has the additional benefit of keeping people engaged in a programme of activity that can ensure that the initial benefits of surgery are maximised and the potential harms of nutritional deficiency are minimised. It was noted from GDG experience that patients often

value support and advice from professionals after surgery (including dietary, physical activity and psychological support) and feel there should be clearer guidance for their primary care physicians about monitoring after surgery and the provision for surgery for excess skin.

Following discharge from the bariatric service

The quality of current services following discharge from the bariatric service varies with the GDG reporting that often the basic service of annual monitoring of nutritional status is being implemented to varying degrees. The GDG felt that the absence of this care in a coherent and consistent manner represented significant risk to the individual who may suffer from long-term harm because of unidentified nutritional deficiencies (such as, Wernicke's encephalopathy, peripheral neuropathy, anaemia, osteoporosis, night blindness, or death) because of a lack of expertise within primary care interpreting blood tests that determine nutritional status. Because of this risk of harm, the GDG chose to make a consensus recommendation in this area.

The GDG felt that the responsibility for lifelong annual follow up after discharge from the bariatric service should be undertaken as part of a shared care model of chronic disease management which the GDG felt should involve collaboration between named tier 3 specialists and primary care. Within this model, a shared care protocol – a clear plan which outlines how the model will be implemented including monitoring arrangements, and responsibilities of the tier 3 specialist, GP and patient – would be developed and followed. As such, the recommendation drafted re-iterates what should be considered routine practice following bariatric surgery.

The GDG felt that in their experience it would be best practice to provide ongoing screening and monitoring of psychological adjustment and wellbeing post bariatric surgery. However they did not feel they could make a specific recommendation about a frequency or recommended time frame for this due to limited available evidence. Instead, the GDG felt that because of the potential for safety issues related to nutritional deficiencies after bariatric surgery, annual monitoring of nutritional status and appropriate supplementation should be an absolute minimum requirement.

The GDG further wished to note that it was their experience that women who have had bariatric surgery have enhanced fertility compared to pre-surgery and that pregnancy (intended or not) is often identified within a 12 month follow- up period in tier 4 services. This group require specialist support so the GDG felt it was important to highlight this potential to all services to manage the risks to mother and baby if access to follow-up care is not taken up.

Finally, the GDG noted the National Confidential Enquiry into Patient Outcome and Death (NCEpod) report which was part of the impetus for prioritising follow-up care after bariatric surgery for this guideline review. The GDG wished to endorse the recommendations that surgery and follow-up data on all those having bariatric surgery should be entered into the National Bariatric Surgery Register. They noted that it was important that data on patients should be submitted each year and that the plan for who should submit data should form part of the shared care management plan.

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11 Acronyms and abbreviations

ABV	Alcohol by volume
BMEG	Black and minority ethnic group
BMI	Body mass index
BT	Behavioural therapy or behavioural treatment
CBA	Controlled before-and-after study
CC	Collaborating centre
CCT	Controlled clinical trial
CHD	Coronary heart disease
CEA	Cost-effectiveness analysis
CG	Clinical guideline
CI	Confidence interval
CPHE	Centre for Public Health Excellence
CUA	Cost-utility analysis
CVD	Cardiovascular disease
DH	Department of Health
EBQ	Evidence-based question
EQ5D	EuroQol 5 dimensions
FBC	Full blood count
GDG	Guideline development group
GP	General practitioner
GPP	Good practice point
GRP	Guideline review panel
HC	High carbohydrate
HDA	Health development agency
HDL	High-density lipoprotein
HP	High protein
HR	Hazard ratio
HRQoL	Health-related quality of life
HTA	Health technology assessment
ICER	Incremental cost-effectiveness ratio
IOTF	International Obesity Taskforce
ITT	Intention to treat
kcal	Calories
LAGB	Laparoscopic (adjustable) gastric banding
LCD	Low-calorie diet
LDL	Low-density lipoprotein
LED	Low-energy diet
LFT	Liver function test
LSP	Local strategic partnership
LYG	Life year gained
MD	Mean difference
MDT	Multidisciplinary team

MID	Minimal important difference
mo	Months
NCC-PC	National Collaborating Centre for Primary Care
NHMRC	National Health and Medical Research Council (Australia)
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NR	Not reported
NSF	National service framework
NSP	Non-starch polysaccharides
OR	Odds ratio
PCT	Primary care trust
PICO	Framework incorporating patients, interventions, comparisons, and outcomes used for the development of evidence-based questions
PSMF	Protein-sparing modified fast
QALY	Quality-adjusted life year
RCT	Randomised control trial
RDA	Recommended daily allowance
RR	Risk ratio or relative risk
SBP	Systolic blood pressure
SD	Standard deviation
SE	Standard error
SEG	Socioeconomic group
SES	Socioeconomic status
SIGN	Scottish Intercollegiate Guidelines Network
VBG	Vertical banded gastroplasty
VLCD	Very-low-calorie diet
VLED	Very-low-energy diet
WC	Waist circumference
WHR	Waist-to-hip ratio
WHO	World Health Organisation
wk	Week
yr	Year

12 Glossary

Abdominoplasty	Plastic surgery of the abdomen in which excess fatty tissue and skin are removed, usually for cosmetic purposes.
Abstract	Summary of a study, which may be published alone or as an introduction to a full scientific paper.
Active play	What children and young people do when they follow their own ideas and interests, in their own way and for their own reasons – such as 'play active games, run about, ride a bike, kick a ball around"(based on Department for Culture Media and Sport definition of play and Health Survey for England 1997 definition of active play).
Active transport/travel	A form of transport that requires physical activity e.g. walking or cycling.
Adiposity	Body fat
Ad libitum diet	No dietary or calorie restrictions
Adult	For the purposes of this guideline, adult is defined as an individual >18 years.* *However it is not considered helpful to have absolute cut offs for ages of children/young persons since the facilities available for the transition of care from child to adult centres can vary between specialities e.g. mental health, endocrinology.
Algorithm (in guidelines)	A flow chart of the clinical decision pathway described in the guideline, where decision points are represented with boxes, linked with arrows.
Allocation concealment	The process used to prevent advance knowledge of group assignment in an RCT. The allocation process should be impervious to any influence by the individual making the allocation, by being administered by someone who is not responsible for recruiting participants.
Anthropometry	Measures of the human body
Applicability	How well the results of a study or NICE evidence review can answer a clinical question or be applied to the population being considered.
Arm (of a clinical study)	Subsection of individuals within a study who receive one particular intervention, for example placebo arm.
Association	Statistical relationship between 2 or more events, characteristics or other variables. The relationship may or may not be causal.
Balanced caloric-deficit diet	A mixed diet containing protein, fat and carbohydrate and providing less energy than energy requirements.
Bariatric surgery	Surgery on the stomach and/or intestines to help the person with extreme obesity lose weight.
Baseline	The initial set of measurements at the beginning of a study (after run-in period where applicable), with which subsequent results are compared.
Behavioural intervention	Refers to the use of the common components of behavioural treatment (self-monitoring, goal setting, stimulus control).
Behavioural treatment	Behavioural treatment (or behaviour therapy) draws on the principles of learning theory (stimulus–behaviour contingencies or behaviour–reward contingencies). Consists of assessment (identifying and specifying problem behaviours and the circumstances in which they are elicited), treatment (including setting specific, measurable and modest goals that are continually revised) and monitoring. Behaviour change processes include stimulus control, graded exposure, extinction and reward.
Beta cells	Produce insulin in response to rising blood glucose levels and mainly regulate the metabolism of carbohydrates, but also of proteins and fats.
Bias	Influences on a study that can make the results look better or worse than

	they really are (bias can even make it look as if a treatment works when it does not). Bias can occur by chance, deliberately or as a result of systematic errors in the design and execution of a study. It can also occur at different stages in the research process: for example, during the collection, analysis, interpretation, publication, or review of research data. For examples see selection bias, confounding factor, and publication bias.
Bilo-pancreatic diversion	A type of weight loss surgery that is similar to a gastric bypass (see below) except that a much larger section of the small intestine is bypassed.
Binge eating disorder (BED)	A syndrome in which an individual experiences repeated uncontrolled episodes of overeating but does not use extreme compensatory weight-control behaviours. Current definitions recognise that this becomes a disorder when binge eating episodes are occurring at least twice a week for a period of 6 months or more. Usually individuals with this disorder feel a compulsion to eat, usually binge eat in private and experience high levels of distress and shame about these behaviours.
Bio-electrical impedance analysis	A way to estimate the amount of body weight that is fat and non-fat. Non-fat weight comes from bone, muscle, body water, organs and other body tissues. BIA works by measuring how difficult it is for a harmless electrical current to move through the body. The more fat a person has, the harder it is for electricity to flow through the body. The less fat a person has, the easier it is for electricity to flow through the body. By measuring the flow of electricity, one can estimate body fat per cent.
Blinding	A way to prevent researchers, doctors and patients in a clinical trial from knowing which study group each patient is in so they cannot influence the results. The best way to do this is by sorting patients into study groups randomly. The purpose of 'blinding' or 'masking' is to protect against bias. A single-blinded study is one in which patients do not know which study group they are in (for example whether they are taking the experimental drug or a placebo). A double-blinded study is one in which neither patients nor the researchers/doctors know which study group the patients are in. A triple blind study is one in which neither the patients, clinicians or the people carrying out the statistical analysis know which treatment patients received.
Body mass index (BMI)	Commonly used to measure whether or not adults are a healthy weight or underweight, overweight or obese. It is defined as the weight in kilograms divided by the square of the height in metres (kg/m2).
BMI z score	BMI z score is a measure of how many standard deviations a child or young person's BMI is above or below the average BMI for their age and gender (this is based on a reference population known as a child growth reference). For instance, a z score of 1.5 indicates that a child is 1.5 standard deviations above the average value, and a z score of −1.5 indicates a child is 1.5 standard deviations below the average value. The advantage of using BMI z scores, instead of BMI, is that it allows direct comparison of BMI (and any changes in BMI) across different ages and by gender. This term is sometimes used interchangeably with 'BMI standard deviation score' (BMI SDS). See the National Obesity Observatory's A simple guide to classifying body mass index in children. Care is needed when interpreting BMI z scores using the UK 1990 centile charts for black, Asian and other minority ethnic groups. There is evidence to suggest that adults from these groups are at risk of obesity-associated conditions and diseases at a lower BMI than the white population.
Bulimia nervosa	A syndrome characterised by recurrent episodes of binge eating and by compensatory behaviour (vomiting, purging, fasting or exercising) in

	order to prevent weight gain. Binge eating is accompanied by a subjective feeling of loss of control over eating. This is a normal weight syndrome in which the body mass index (BMI) is maintained above 17.5 kg/m2.
Calorie value	The number of calories (kcal) in any given food or drink. Fat provides 9 calories per gram, alcohol provides 7 calories per gram, carbohydrates and proteins provide 4 calories per gram. 1 kcal = 4.2 kilojoules (kJ).
Carer (caregiver)	Someone who looks after family, partners or friends in need of help because they are ill, frail or have a disability.
Case series	Report of a number of cases of a given disease, usually covering the course of the disease and the response to treatment. There is no comparison (control) group of patients.
Child	For the purposes of this guidance, child is defined as an individual aged <18 years* *However, it is not considered helpful to have absolute cut-offs for ages of children/young persons since the facilities available for the transition of care from child to adult centres can vary between specialties e.g. mental health, endocrinology.
Cholelithiasis	See gallstones
Clinical effectiveness	How well a specific test or treatment works when used in the 'real world' (for example, when used by a doctor with a patient at home), rather than in a carefully controlled clinical trial. Trials that assess clinical effectiveness are sometimes called management trials. Clinical effectiveness is not the same as efficacy.
Clinician	A healthcare professional who provides patient care. For example: a doctor, nurse, or physiotherapist.
Cochrane Review	The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of randomised controlled trials prepared by the Cochrane Collaboration).
Cohort study	A retrospective or prospective follow-up study. Groups of individuals to be followed up are defined on the basis of presence or absence of exposure to a suspected risk factor or intervention. A cohort study can be comparative, in which case 2 or more groups are selected on the basis of differences in their exposure to the agent of interest.
Comorbidities	Comorbidities are diseases or conditions that someone has in addition to the health problem being studied or treated. Some comorbidities, such as type 2 diabetes, are associated with being overweight or obese, because the risk of developing them increases with an increasing BMI.
Complex obesity	Complex obesity occurs when someone who is obese has additional and related diseases or conditions, for example, type 2 diabetes. It can also occur when obesity results from an underlying condition, for example, an endocrine disease or condition, or when it is associated with various syndromes (such as Prader-Willi syndrome). Complex obesity can occur regardless of how obese the person is, although it is more likely as BMI increases.
Confidence interval (CI)	There is always some uncertainty in research. This is because a small group of patients is studied to predict the effects of a treatment on the wider population. The confidence interval is a way of expressing how certain we are about the findings from a study, using statistics. It gives a range of results that is likely to include the 'true' value for the population. The CI is usually stated as '95% CI', which means that the range of values has a 95 in a 100 chance of including the 'true' value. For example, a study may state that 'based on our sample findings, we are 95% certain that the 'true' population blood pressure is not higher than 150 and not lower than 110'. In

	such a case the 95% CI would be 110 to 150. A wide confidence interval indicates a lack of certainty about the true effect of the test or treatment - often because a small group of patients has been studied. A narrow confidence interval indicates a more precise estimate (for example, if a large number of patients have been studied).
Confounding factor	Something that influences a study and can result in misleading findings if it is not understood or appropriately dealt with. For example, a study of heart disease may look at a group of people that exercises regularly and a group that does not exercise. If the ages of the people in the 2 groups are different, then any difference in heart disease rates between the 2 groups could be because of age rather than exercise. Therefore, age is a confounding factor.
Consensus methods	Techniques used to reach agreement on a particular issue. Consensus methods may be used to develop NICE guidance if there is not enough good quality research evidence to give a clear answer to a question. Formal consensus methods include Delphi and nominal group techniques.
Constipation	A term to describe the subjective complaint of passage of abnormally delayed or infrequent passage of dry, hardened faeces often accompanied by straining and/or pain.
Control group	A group of people in a study who do not receive the treatment or test being studied. Instead, they may receive the standard treatment (sometimes called 'usual care') or a dummy treatment (placebo). The results for the control group are compared with those for a group receiving the treatment being tested. The aim is to check for any differences. Ideally, the people in the control group should be as similar as possible to those in the treatment group, to make it as easy as possible to detect any effects due to the treatment.
Cost–benefit analysis (CBA)	Cost-benefit analysis is one of the tools used to carry out an economic evaluation. The costs and benefits are measured using the same monetary units (for example, pounds sterling) to see whether the benefits exceed the costs.
Cost-effectiveness analysis (CEA)	Cost-effectiveness analysis is one of the tools used to carry out an economic evaluation. The benefits are expressed in non-monetary terms related to health, such as symptom-free days, heart attacks avoided, deaths avoided, or life years gained (that is, the number of years by which life is extended as a result of the intervention).
Cost-effectiveness model	An explicit mathematical framework which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes.
Cost–utility analysis (CUA)	Cost-utility analysis is one of the tools used to carry out an economic evaluation. The benefits are assessed in terms of both quality and duration of life, and expressed as quality-adjusted life years (QALYs). See also utility.
C-peptide	Biologically inactive part of pro-insulin molecule, secreted in equal molar quantities with insulin. C-peptide level gives information on endogenous insulin secretion.
Depression	Depression is a broad and heterogeneous diagnosis. Central to it is depressed mood and/or loss of pleasure in most activities. A chronic physical health problem can both cause and exacerbate depression: pain, functional impairment and disability associated with chronic physical health problems can greatly increase the risk of depression in people with physical illness. Depression can also exacerbate the pain and distress associated with physical illnesses and adversely affect outcomes, including shortening life expectancy.
Diabesity	A popular term for the association of type 2 diabetes mellitus and obesity.

Diabetes mellitus	Chronic condition characterised by elevated blood glucose levels. Diabetes is of diverse aetiology and pathogenesis, and should not be regarded as a single disease. Predominant types are Type 1 diabetes and Type 2 diabetes, diabetes secondary to other pancreatic disease or other endocrine disease, and diabetes of onset in pregnancy.
Diarrhoea	A condition in which the sufferer has frequent and watery or loose bowel movements (from the ancient Greek word διαρροή = leakage; lit. "to run through").
Diet	The habitual food intake of people or animals or A plan of food and drink set down for the loss of weight, or a prescribed plan for medical reasons.
Disordered eating	Refers to a range of irregular eating behaviours that have not been given a specific diagnosis of eating disorder such as anorexia nervosa or bulimia nervosa.
Drop-out	A participant who withdraws from a trial before the end.
Dumping syndrome	A set of symptoms that can affect people after a gastrectomy. It is caused when particularly sugary or starchy food moves suddenly into the small intestine.
Duodenal switch	A type of weight loss surgery in which the size of the stomach is reduced, leaving in place the pylorus and a little of the duodenum which is anastomosed (or joined to the ileum).
Economic evaluation	An economic evaluation is used to assess the cost effectiveness of healthcare interventions (that is, to compare the costs and benefits of a healthcare intervention to assess whether it is worth doing). The aim of an economic evaluation is to maximise the level of benefits - health effects - relative to the resources available. It should be used to inform and support the decision-making process; it is not supposed to replace the judgement of healthcare professionals. There are several types of economic evaluation: cost-benefit analysis, cost-consequence analysis, cost-effectiveness analysis, cost-minimisation analysis and cost-utility analysis. They use similar methods to define and evaluate costs, but differ in the way they estimate the benefits of a particular drug, programme or intervention.
Effect (as in effect measure, treatment effect, estimate of effect, effect size)	A measure that shows the magnitude of the outcome in one group compared with that in a control group. For example, if the absolute risk reduction is shown to be 5% and it is the outcome of interest, the effect size is 5%. The effect size is usually tested, using statistics, to find out how likely it is that the effect is a result of the treatment and has not just happened by chance (that is, to see if it is statistically significant).
Effectiveness	How beneficial a test or treatment is under usual or everyday conditions, compared with doing nothing or opting for another type of care.
Efficacy	How beneficial a test, treatment or public health intervention is under ideal conditions (for example, in a laboratory), compared with doing nothing or opting for another type of care.
Energy-dense food	Food and drinks which provide relatively high amounts of calories per gram, millilitre and/or serving. The World Health Organization (2003) states that energy-dense foods 'tend to be processed foods that are high in fat and/or sugar. Low energy-dense (or energy dilute) foods such as fruit, legumes, vegetables and whole grain cereals are high in dietary fibre and water.'
EQ-5D (EuroQol 5	A standardised instrument used to measure health-related quality of life. It

dimensions)	provides a single index value for health status.
Evidence	Information on which a decision or guidance is based. Evidence is obtained from a range of sources including randomised controlled trials, observational studies, expert opinion (of clinical professionals or patients).
Exclusion criteria (literature review)	Explicit standards used to decide which studies should be excluded from consideration as potential sources of evidence.
Exclusion criteria (clinical study)	Criteria that define who is not eligible to participate in a clinical study.
Exercise	Planned bouts of physical activity usually pursued for personal health and fitness goals. Exercise is a subset of physical activity, which is planned, structured, and repetitive. It is aimed at improving or maintaining any aspect of fitness or health.
Extrapolation	An assumption that the results of studies of a specific population will also hold true for another population with similar characteristics.
Fast foods	No specific definition but commonly used slang term for foods which are generally sold in retail outlets and which are high in calories, fat, saturated fat, sugar and/or salt.
Fatty acids	Organic acids containing carbon, hydrogen, and oxygen. Fatty acids are an important component of lipids (fat-soluble components of living cells).
Fatty foods	Foods high in total fat and/or saturated fat. The Food Standards Agency (FSA) provides the following guidance: 20g fat or more per 100g is a lot of fat 5g saturates or more per 100g is a lot 3g fat or less per 100g is a little fat 1g saturates or less per 100g is a little fat.
Follow-up	Observation over a period of time of an individual, group or initially defined population whose appropriate characteristics have been assessed in order to observe changes in health status or health-related variables.
Gallstones	Small stones, usually made of cholesterol, that form in the gallbladder.
Gastrectomy	Surgical removal of all or part of the stomach.
Gastric balloon	A soft silicone balloon that is surgically implanted into the stomach. The balloon is filled with air or saline solution (sterile salt water), and so takes up some of the space in the stomach.
Gastric band	A type of weight loss surgery that reduces the capacity of the stomach using an adjustable band.
Gastric bypass	A type of weight loss surgery that reduces the size of the stomach and shortens the length of the small intestine that food passes through.
Gastrostomy	Enteral tube inserted through the abdominal wall into the stomach for the purpose of nutrition support.
Glucose	Glucose comes from digesting carbohydrate and is also produced by the liver. Carbohydrate comes from many different kinds of food and drink, including starchy foods such as bread, potatoes and chapatis; fruit; some dairy products; sugar and other sweet foods (Diabetes UK 2010).
Glycaemic control	The regulation and maintenance of blood glucose levels within normal ranges.
Glycated haemoglobin (HbA1c)	Forms when red cells are exposed to glucose in the plasma. The HbA1c test reflects average plasma glucose over the previous 8 to 12 weeks. Unlike the oral glucose tolerance test, an HbA1c test can be performed at any time of the day and does not require any special preparation such as fasting. HbA1c is a continuous risk factor for type 2 diabetes. This means there is no fixed point when people are or are not at risk. The World Health Organization recommends a level of 6.5% (48 mmol/mol) for HbA1c as the cut-off point

	for diagnosing type 2 diabetes in non-pregnant adults.
Gout	A type of arthritis where crystals of sodium urate form inside and around joints.
GRADE, GRADE profile	A system developed by the GRADE Working Group to address the shortcomings of present grading systems in healthcare. The GRADE system uses a common, sensible and transparent approach to grading the quality of evidence. The results of applying the GRADE system to clinical trial data are displayed in a table known as a GRADE profile.
Harms	Adverse effects of an intervention.
Health economics	Study or analysis of the cost of using and distributing healthcare resources.
Health-related quality of life (HRQoL)	A measure of the effects of an illness to see how it impacts upon someone's day-to-day life.
Healthy diet	A healthy diet contains plenty of fruit and vegetables; is based on starchy foods such as wholegrain bread, pasta and rice; and is low in fat (especially saturated fat), salt and sugar. Specific dietary recommendations (UK) (Population average intakes; apply to children aged 5 years and over) Total fat: maintain at 35% of food energy Saturated fat: reduce to 11% of food energy Added sugar: reduce to 11% of food energy Fibre: increase to 18g/day Salt: reduce to no more than 6g/day* Fruit and vegetables: increase consumption of a variety of fruit and vegetables to at least 5 portions per day. *1The maximum amount of salt recommended for children is less than that for adults – see www.eatwell.gov.uk for specific recommendations.
Healthy weight	A person who has a body mass index (BMI) 18.5-24.9.
Heterogeneity or Lack of homogeneity	The term is used in meta-analyses and systematic reviews to describe when the results of a test or treatment (or estimates of its effect) differ significantly in different studies. Such differences may occur as a result of differences in the populations studied, the outcome measures used or because of different definitions of the variables involved. It is the opposite of homogeneity.
Hypertension	High blood pressure
Hypoglycaemia	Low blood glucose level
Impaired glucose tolerance	This is a risk factor for future diabetes and/or other adverse outcomes. The current WHO diagnostic criteria for impaired glucose tolerance are: a fasting plasma glucose of less than 7.0 mmol/l and a 2-hour venous plasma glucose (after ingestion of 75 g oral glucose load) of 7.8 mmol/l or greater, and less than 11.1 mmol/l.
Imprecision	Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of effect.
Inclusion criteria (literature review)	Explicit criteria used to decide which studies should be considered as potential sources of evidence.
Incremental cost	The extra cost linked to using one test or treatment rather than another. Or the additional cost of doing a test or providing a treatment more frequently.
Incremental cost-effectiveness ratio (ICER)	The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest for one treatment compared with another.
Indirectness	The available evidence is different to the review question being addressed,

	in terms of PICO (population, intervention, comparison and outcome).
Insulin	Insulin is the hormone produced by the pancreas that allows glucose to enter the body's cells, where it is used as fuel for energy. It is vital for life (Diabetes UK 2010).
Intermediate outcomes	Results or outcomes of action that must occur prior to the final outcome and in order to produce the final outcome. Within the context of this work, relevant changes in diet or activity levels may be considered intermediate outcomes for the assessment of interventions to prevent weight or manage obesity.
Intervention	In medical terms this could be a drug treatment, surgical procedure, diagnostic or psychological therapy. Examples of public health interventions could include action to help someone to be physically active or to eat a more healthy diet.
Laparoscopic sleeve gastrectomy	See sleeve gastrectomy
Life-long learning	A continuum of the learning process that takes place at all levels - formal, non-formal and informal - utilizing various modalities such as distance learning and conventional learning.
Lifestyle activity	Activities that are performed as part of everyday life, such as climbing stairs, walking (for example, to work, school or shops) and cycling. They are normally contrasted with 'programmed' activities such as attending a dance class or fitness training session.
Life years gained	Mean average years of life gained per person as a result of the intervention compared with an alternative intervention.
Long-term	For the purposes of this guidance, long-term is considered 1 year or more.
Low-calorie diet	A weight loss diet containing less energy than an individual's energy needs – typically 1000-1500 kilocalories per day.
Low-fat diet	A diet where 30% or less of the total daily energy is derived from fat.
Markov model	A method for estimating long-term costs and effects for recurrent or chronic conditions, based on health states and the probability of transition between them within a given time period (cycle).
Meta-analysis	A method often used in systematic reviews. Results from several studies of the same test or treatment are combined to estimate the overall effect of the treatment.
Metabolic equivalent (MET)	1 MET = a person's metabolic rate (rate of energy expenditure) when at rest. MET values are assigned to activities to denote their intensity and are given in multiples of resting metabolic rate. For example, walking elicits an intensity of 3–6 METs, depending on how brisk the walk is, and more strenuous activity such as running would have an intensity of 7–10 METs.
Multicomponent intervention	An intervention that aims to address a range of factors which may influence the outcome measure of interest. Sometimes referred to as 'multifaceted'.
Night eating syndrome (NES)	Primarily characterises a persistent and ongoing pattern of late-night eating, with more than 25% of a person's calorific intake occurring after the evening meal and associated nocturnal awakening and food ingestion occurring at least 2 or 3 times per week .
Observational study	An epidemiological study that does not involve any intervention, experimental or otherwise. Nature is allowed to take its course with changes in one characteristic being studied in relation to changes in other characteristics.
Oral glucose tolerance test (OGTT)	Involves measuring the blood glucose level after fasting, and then 2 hours after drinking a standard 75g glucose drink. Fasting is defined as no calorie intake for at least 8 hours. More than one test on separate days is required for diagnosis in the absence of hyperglycaemic symptoms.

Outcome	The impact that a test, treatment, policy, programme or other intervention has on a person, group or population. Outcomes from interventions to improve the public's health could include changes in knowledge and behaviour related to health, societal changes (for example, a reduction in crime rates) and a change in people's health and wellbeing or health status. In clinical terms, outcomes could include the number of patients who fully recover from an illness or the number of hospital admissions, and an improvement or deterioration in someone's health, functional ability, symptoms or situation. Researchers should decide what outcomes to measure before a study begins.
P value	The p value is a statistical measure that indicates whether or not an effect is statistically significant. For example, if a study comparing 2 treatments found that one seems more effective than the other, the p value is the probability of obtaining these results by chance. By convention, if the p value is below 0.05 (that is, there is less than a 5% probability that the results occurred by chance) it is considered that there probably is a real difference between treatments. If the p value is 0.001 or less (less than a 1% probability that the results occurred by chance), the result is seen as highly significant. If the p value shows that there is likely to be a difference between treatments, the confidence interval describes how big the difference in effect might be.
Perioperative	The period from admission through surgery until discharge, encompassing the pre-operative and post-operative periods.
Physical activity	The full range of human movement, from competitive sport and exercise to active hobbies, walking, cycling or activities of daily living. Physical activity varies by: Volume or quantity (total quantity of physical activity over a specified period, usually expressed as kcal or METs per day or week); Frequency of participation, typically expressed as number of sessions per day or week; Intensity, usually expressed as light, moderate or vigorous. Commonly used approximations are: light intensity = less than 4 METs, for example, strolling; moderate = 4 – 6 METs, for example, brisk walking, vigorous = 7+ METs for example, running; Duration – time spent on a single bout of activity; Type or mode – qualitative descriptor such as brisk walking, dancing or weight training.
Physical literacy	Motivation, confidence, physical competence, understanding and knowledge to maintain physical activity at an individually appropriate level, throughout life.
Placebo	A fake (or dummy) treatment given to participants in the control group of a clinical trial. It is indistinguishable from the actual treatment (which is given to participants in the experimental group). The aim is to determine what effect the experimental treatment has had over and above any placebo effect caused because someone has received (or thinks they have received) care or attention.
Postoperative	Pertaining to the period after patients leave the operating theatre, following surgery.
Postural hypotension	Condition (also known as orthostatic hypotension) in which a marked fall in blood pressure is provoked by a change in posture from lying to sitting or from lying or sitting to standing. This may cause lightheadedness (“dizziness”), a fall, or transient loss of consciousness (blackout).
Preoperative	The period before surgery commences.

Primary care	Healthcare delivered outside hospitals. It includes a range of services provided by GPs, nurses, health visitors, midwives and other healthcare professionals and allied health professionals such as dentists, pharmacists and opticians.
Protein-sparing modified fast	A diet which is relatively high in protein (0.8-1.5g/kg of ideal body weight (IWB) per day), low fat and low carbohydrates. It is hypocaloric and generally contains fewer than 800 kilocalories per day. It contains supplements to meet the dietary reference values for vitamins and minerals. Often recommended only for short-term use in individuals who are obese.
Psychosocial	Involving aspects of social and psychological behaviour or experience
Publication bias	Publication bias occurs when researchers publish the results of studies showing that a treatment works well and don't publish those showing it did not have any effect. If this happens, analysis of the published results will not give an accurate idea of how well the treatment works. This type of bias can be assessed by a funnel plot.
Quality of life	See 'Health-related quality of life'.
Quality-adjusted life year (QALY)	A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. One QALY is equal to 1 year of life in perfect health. QALYS are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a quality of life score (on a scale of 0 to 1). It is often measured in terms of the person's ability to perform the activities of daily life, freedom from pain and mental disturbance.
Quasi-experimental study	A study in which some subjects receive an experimental prevention or therapeutic product or intervention and are compared with subjects who do not, but allocation to each of the groups is not random.
Randomisation	Assigning participants in a research study to different groups without taking any similarities or differences between them into account. For example, it could involve using a random numbers table or a computer-generated random sequence. It means that each individual (or each group in the case of cluster randomisation) has the same chance of receiving each intervention.
Randomised controlled trial (RCT)	A comparative study in which participants are randomly allocated to intervention and control groups and followed up to examine differences in outcomes between the groups.
RCT	See 'Randomised controlled trial'.
Recent onset diabetes	Defined for the purposes of this guideline as within 10 years of diagnosis.
Red food	From Epstein and coworkers' traffic light diet. Consists of high in calories, low in nutrient density foods.
Relative risk (RR)	The ratio of the risk of disease or death among those exposed to certain conditions compared with the risk for those who are not exposed to the same conditions (for example, the risk of people who smoke getting lung cancer compared with the risk for people who do not smoke). If both groups face the same level of risk, the relative risk is 1. If the first group had a relative risk of 2, subjects in that group would be twice as likely to have the event happen. A relative risk of less than 1 means the outcome is less likely in the first group. Relative risk is sometimes referred to as risk ratio.
Review question	In guideline development, this term refers to the questions about treatment and care that are formulated to guide the development of evidence-based recommendations.

Revisional surgery	Bariatric procedure performed to correct or modify a previous bariatric procedure.
Selection bias	Selection bias occurs if: a) The characteristics of the people selected for a study differ from the wider population from which they have been drawn, or b) There are differences between groups of participants in a study in terms of how likely they are to get better.
Sensitivity	How well a test detects the thing it is testing for. If a diagnostic test for a disease has high sensitivity, it is likely to pick up all cases of the disease in people who have it (that is, give a 'true positive' result). But if a test is too sensitive it will sometimes also give a positive result in people who don't have the disease (that is, give a 'false positive'). For example, if a test were developed to detect if a woman is 6 months pregnant, a very sensitive test would detect everyone who was 6 months pregnant, but would probably also include those who are 5 and 7 months pregnant. If the same test were more specific (sometimes referred to as having higher specificity), it would detect only those who are 6 months pregnant, and someone who was 5 months pregnant would get a negative result (a 'true negative'). But it would probably also miss some people who were 6 months pregnant (that is, give a 'false negative'). Breast screening is a 'real-life' example. The number of women who are recalled for a second breast screening test is relatively high because the test is very sensitive. If it were made more specific, people who don't have the disease would be less likely to be called back for a second test but more women who have the disease would be missed.
Sensitivity analysis	A means of representing uncertainty in the results of economic evaluations. Uncertainty may arise from missing data, imprecise estimates or methodological controversy. Sensitivity analysis also allows for exploring the generalisability of results to other settings. The analysis is repeated using different assumptions to examine the effect on the results. One-way simple sensitivity analysis (univariate analysis): each parameter is varied individually in order to isolate the consequences of each parameter on the results of the study. Multi-way simple sensitivity analysis (scenario analysis): 2 or more parameters are varied at the same time and the overall effect on the results is evaluated. Threshold sensitivity analysis: the critical value of parameters above or below which the conclusions of the study will change are identified. Probabilistic sensitivity analysis: probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (for example, Monte Carlo simulation).
Serum uric acid level	The amount of uric acid in the blood.
Short-term	For the recommendations in this guidance, short-term is defined as less than 1 year.
Shared care model	Joint participation of GPs and named tier 3 specialists in the planned delivery of care for a person with chronic disease. It involves an enhanced exchange of information over and above routine referral notices.
Shared care protocol	A clear plan of care for implementing a shared care model, with a defined statement of monitoring arrangements, and responsibilities of the tier 3 specialist, GP and patient. This should include monitoring of blood, nutritional status, and chronic disease management.
Significance (statistical)	A result is deemed statistically significant if the probability of the result occurring by chance is less than 1 in 20 ($p<0.05$).

Skinfold thickness	A measure of the amount of fat under the skin; the measurement is made with a calliper. Measurements at several sites are normally required as the per cent of fat at each site varies with age, sex and ethnicity. Skinfold measurements are usually taken at the triceps, subscapular and supra-iliac sites.
Sleeve gastrectomy	Also known as laparoscopic sleeve gastrectomy or gastric sleeve, sleeve gastrectomy is a type of weight loss surgery in which a section of the stomach is removed.
Snack	No specific definition. Foods consumed between meals or instead of a main meal.
Social marketing	The application of commercial marketing technologies to the analysis, planning, execution, and evaluation of programmes designed to influence the voluntary behaviour of target audiences to improve their personal welfare and that of their society.
Stakeholder	An organisation with an interest in a topic that NICE is developing a clinical guideline or piece of public health guidance on. Organisations that register as stakeholders can comment on the draft scope and the draft guidance. Stakeholders may be: manufacturers of drugs or equipment national patient and carer organisations NHS organisations organisations representing healthcare professionals.
Sugary foods and drinks	Food and drinks high in added sugars. The FSA provides the following guidance: 10 g sugar or more per 100 g is A LOT of sugar 2 g sugar or less per 100 g is A LITTLE sugar.
Systematic review	A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to predetermined criteria. It may include a meta-analysis.
Tiered services	Different tiers of weight management services cover different activities. Definitions vary locally but usually tier 1 covers universal services (such as health promotion or primary care); tier 2 covers lifestyle interventions; tier 3 covers specialist weight management services; and tier 4 covers bariatric surgery.
Time horizon	The timespan over which costs and health outcomes are considered in a decision analysis or economic evaluation.
Traffic light diet	This is a calorie-based food-exchange system created by Epstein and coworkers. Foods are divided into 5 groups (fruits and vegetables, grains, proteins, dairy and other foods), and the foods in each group are colour coded according to nutrient density: green for 'go', yellow for 'eat with care', and red for 'stop'. Green foods are foods containing less than 20 calories per serving, yellow foods are the staple of the diet and provide most of the basic nutrition and red foods are those foods high in fat and simple carbohydrates. All sweets and sugared beverages are classified as red foods. Families are then instructed to count calories and cannot have more than 4 red foods a week.
Travel plan	Department for Transport definition: A travel plan is a package of measures produced by employers to encourage staff to use alternatives to single-occupancy car use. Such a plan could include: car sharing schemes; a commitment to improve cycling facilities; a dedicated bus service or restricted car parking allocations. It might also promote flexible working practices such as remote access and video conferencing.

Type 1 diabetes	Insulin-deficiency disease, developing predominantly in childhood, characterized by hyperglycaemia if untreated, and with a consequent high risk of vascular damage developing over a period of decades.
Type 2 diabetes	Diabetes generally of slow onset mainly found in adults and in association with features of the metabolic syndrome. Carries a very high risk of vascular disease. While not insulin-dependent, many people with the condition eventually require insulin therapy for optimal blood glucose control.
Utility	In health economics, a 'utility' is the measure of the preference or value that an individual or society places upon a particular health state. It is generally a number between 0 (representing death) and 1 (perfect health). The most widely used measure of benefit in cost-utility analysis is the quality-adjusted life year, but other measures include disability-adjusted life years (DALYs) and healthy year equivalents (HYEs).
Very-low-calorie diet	Hypocaloric diets which provide between 450 to 800 kcal per day and are relatively enriched in protein of high biological value. They must contain the full complement of vitamins, minerals, electrolytes and fatty acids. They are usually in a liquid formulation and intended to completely replace food intake in a weight loss programme for a specific period of time.
Vulnerable groups	Populations who face a greater than average risk of weight gain due to a range of factors largely beyond their control. Some of these factors may be inherent, while others may relate to the social, economic and environmental circumstances in which they live.
Waist-to-hip ratio	Waist circumference (cm) divided by hip circumference (cm). Provides a proxy measure of central distribution of fat (intra-abdominal fat).