National Clinical Guideline Centre

# Obesity

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

*Update of CG43*

*Appendix C*

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Royal College of Physicians
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# Appendix C: Review protocols

## C.1 Clinical evidence reviews

### C.1.1 Very-low-calorie diets (VLCD)

#### C.1.1.1 Effectiveness

| Review question | In people who are overweight or obese, what is the clinical and cost effectiveness of very-low-calorie diets in reducing weight? |
|---|---|
| Guideline condition and its definition | Obese and overweight. Definition: Overweight: 25-29.9 BMI (kg/m2) Obese: >30 BMI (kg/m2) |
| Objectives | To examine the effectiveness of very-low-calorie diets in the treatment of obesity – focusing on adherence and sustainability of weight loss. |
| Review population | Overweight and obese adults and children |
| Population | Adults (18 years old and over)<br>Children (over 2 years)<br><br>(if no data on children or young people, the GDG will consider extrapolating from the adult population for these groups) |
| | Line of therapy not an inclusion criterion |
| Interventions and comparators: generic/class; specific/drug<br><br>(All interventions will be compared with each other, unless otherwise stated) | Intervention: Very-low-calorie diet (≤800 calories per day) – nutritionally complete, meal replacement, minerals, see scoop guidelines 2002 – bench mark for diets, need to comply with this guidance. Also referred to as VLED (very low energy diets). Includes intermittent diets (i.e. just 2 days a week – usually 8 weeks LVCD and then intermittent). Report delivery, intensity of delivery, how and who delivered.<br><br>Comparison: Standard dietary advice defined as a low-calorie (regular) diet (LCD) - 800-1600 calories per day or 500/800 deficit diet.<br><br>Need to report and/minus exercise advice/multicomponent psychological support. |
| Outcomes (& any minimally important differences; default MIDs will be used unless otherwise stated) | Effectiveness:<br><br>% weight in kg change (from start of study to end of maintenance period) (continuous) CRITICAL<br>Health related quality of life (continuous) CRITICAL<br>Withdrawals (dichotomous) CRITICAL<br>Weight in BMI, change (from start of study to end of maintenance period) - % reduction IMPORTANT<br>Weight change at end of VLCD to end of maintenance period - % kg (continuous) IMPORTANT<br>Weight change at end of diet to end of maintenance period - % BMI (continuous) IMPORTANT<br>Improvement in physical activity (continuous) IMPORTANT |
| Study design | RCT<br>Systematic Review of RCTS |

| Review question | In people who are overweight or obese, what is the clinical and cost effectiveness of very-low-calorie diets in reducing weight? |
|---|---|
| | (conference abstracts if no evidence) |
| Unit of randomisation | Patient |
| Crossover study | Not permitted |
| Minimum duration of study | 1 year |
| Other exclusions | Pregnant women<br>Children under 2 years old<br>People of a healthy weight<br>People not on a very-low-calorie diet<br>Non-English language studies<br>Abstracts (excluded from the review, not the search) |
| Population stratification | None |
| Reasons for stratification | Intervention is likely to have a different effect on different BMI thresholds |
| Other stratifications | Type of diet but they will be combined |
| Sensitivity/other analysis | Combined studies across different types of studies<br>Dichotomous data for time-to-event outcomes (at <1 year, 1year - 2years, 2 years - 3 years) |
| Subgroup analyses if there is heterogeneity | - T2DM (T2DM; Non-diabetic people); Expect VLCD to have different outcomes in people with T2DM<br>- Ethnicity (White (>80%); Asian (>80%); Black (>80%)); Expect VLCD to have different outcomes in different ethnicities<br>- Diet (Supervised VLCD; Non-supervised VLCD); Expect VLCD to work better in people who have followed a supervised diet<br><br>People with learning disabilities<br>People osteoarthritis, sleep apnoea, giving up smoking |
| Search criteria | Databases: Medline, Embase, the Cochrane Library<br>Date limits for search: None<br>Language: English language only (except studies translated for Cochrane reviews or as directed by the GDG) |

### C.1.1.2 Safety

| 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? |
|---|---|
| Guideline condition and its definition | Obese and overweight. Definition: Overweight: 25-29.9 BMI (kg/m2) Obese: >30 BMI (kg/m2) |
| Objectives | To examine the safety of very-low-calorie diets in the treatment of obesity |
| Review population | Overweight and obese adults and children – after a baseline VLCD period |
| | As above |
| | Line of therapy not an inclusion criterion |
| Interventions and comparators: generic/class; specific/drug<br><br>(All interventions will be | Intervention: Very-low-calorie diet (800 or below calories per day) – nutritionally complete, meal replacement, minerals, see scoop guidelines 2002 – bench mark for diets, need to comply with this guidance. Also referred to as VLED (very-low-energy diets).<br>Includes intermittent diets (i.e. just 2 days a week – usually 8 weeks LVCD and then intermittent). |

| 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? |
|---|---|
| compared with each other, unless otherwise stated) | Report delivery, intensity of delivery, how and who delivered.<br><br>Comparison: Standard dietary advice defined as a low-calorie (regular) diet (LCD) - above 800-1600 calories per day or 500/800 deficit diet.<br><br>Need to report and/minus exercise advice/multicomponent psychological support. |
| Outcomes (& any minimally important differences; default MIDs will be used unless otherwise stated) | Disordered eating (dichotomous/continuous) CRITICAL<br>Depression score (continuous) CRITICAL<br>Postural hypotension (dichotomous) CRITICAL<br><br>Bone density (continuous) IMPORTANT<br>Constipation (dichotomous) IMPORTANT<br>Gallstones (dichotomous) IMPORTANT<br>Gout measured by Increase serum uric acid levels (dichotomous/continuous) IMPORTANT<br>Diarrhoea (dichotomous) IMPORTANT<br>Hypoglycaemia (dichotomous) IMPORTANT |
| Study design | RCT<br>Systematic Review of RCTs<br>(conference abstracts if no evidence) |
| Unit of randomisation | Patient |
| Crossover study | Not permitted |
| Minimum duration of study | None |
| Other exclusions | Pregnant women<br>Children under 2 years old<br>People of a healthy weight<br>People not on a very-low-calorie diet<br>Non-English language studies<br>Abstracts (excluded from the review, not the search) |
| Population stratification | None |
| Reasons for stratification | Intervention is likely to have a different effect on different BMI thresholds |
| Other stratifications | Type of diet but they will be combined |
| Sensitivity/other analysis | Combined studies across different types of studies<br>Dichotomous data for time-to-event outcomes (at <1 year, 1year - 2years, 2 years - 3 years) |
| Subgroup analyses if there is heterogeneity | As above |
| Search criteria | Databases: Medline, Embase, the Cochrane Library<br>Date limits for search: None<br>Language: English language only (except studies translated for Cochrane reviews or as directed by the GDG) |

### C.1.1.3 Maintenance

| Review question | What are effective management strategies for maintaining weight loss after very-low-calorie diets in people who are overweight or obese? |
|---|---|
| Guideline condition and its definition | Obese and overweight. Definition: Overweight: 25-29.9 BMI (kg/m2) Obese: >30 BMI (kg/m2) |
| Objectives | To examine the effectiveness of maintaining weight loss after a very-low-calorie diet in the treatment of obesity |
| Review population | Overweight and obese adults and children |
| Population | Adults (18 years old and over)<br>Children (over 2 years)<br><br>(if no data on children or young people, the GDG will consider extrapolating from the adult population for these groups) |
| | Line of therapy not an inclusion criterion |
| Interventions and comparators: generic/class; specific/drug<br><br>(All interventions will be compared with each other, unless otherwise stated) | All patients have a lead-in period on a VLCD (<800 calories) for 6-12 weeks before randomisation.<br><br>Intervention: maintenance strategy:<br>Anti-obesity drugs<br>Exercise<br>Diet<br>Combinations of above<br><br>Comparison:<br>Standard dietary advice (control)<br>Placebo<br>Other maintenance strategies |
| Outcomes (& any minimally important differences; default MIDs will be used unless otherwise stated) | % weight change (kg) from end of VLCD to end of study (Continuous)<br>Health related quality of life (Continuous)<br>% drop outs (Adherence)<br>% weight change (BMI) from end of VLCD to end of study (continuous)<br>% weight change from before VLCD to end of study (kg)<br>% weight change from before VLCD to end of study (BMI)<br>Improvement in physical activity |
| Study design | RCT<br>Systematic Review of RCTS<br>(conference abstracts if no evidence) |
| Unit of randomisation | Patient |
| Crossover study | Not permitted |
| Minimum duration of study | 1 year |
| Other exclusions | Pregnant women<br>Children under 2 years old<br>People of a healthy weight<br>People not on a very-low-calorie diet<br>Non-English language studies<br>Abstracts (excluded from the review, not the search) |
| Population stratification | None |

| Review question | What are effective management strategies for maintaining weight loss after very-low-calorie diets in people who are overweight or obese? |
|---|---|
| Reasons for stratification | Intervention is likely to have a different effect on different BMI thresholds |
| Other stratifications | Type of diet but they will be combined |
| Sensitivity/other analysis | Combined studies across different types of studies<br>Dichotomous data for time-to-event outcomes (at <1 year, 1year - 2years, 2 years - 3 years) |
| Subgroup analyses if there is heterogeneity | - T2DM (T2DM; Non-diabetic people); Expect VLCD to have different outcomes in people with T2DM<br>- Ethnicity (White (>80%); Asian (>80%); Black (>80%)); Expect VLCD to have different outcomes in different ethnicities<br>- Diet (Supervised VLCD; Non-supervised VLCD); Expect VLCD to work better in people who have followed a supervised diet<br><br>People with learning disabilities<br>People with osteoarthritis, sleep apnoea, giving up smoking |
| Search criteria | Databases: Medline, Embase, the Cochrane Library<br>Date limits for search: None<br>Language: English language only (except studies translated for Cochrane reviews or as directed by the GDG) |

### C.1.2 Bariatric surgery in people with type 2 diabetes

| 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? |
|---|---|
| Guideline condition and its definition | Obese and overweight. Definition: Overweight: 25-29.9 BMI (kg/m2) Obese: >30 BMI (kg/m2) |
| Objectives | Should bariatric surgery be a first line therapy for type 2 diabetes patients who are obese and overweight? |
| Review population | Type 2 diabetes, new onset (duration less than or equal to 10 years) and obese/overweight |
| | Adults (19 years old and over)<br>Young people (16-18 years old)<br>Children (2-15 years old)<br>Mixed age (over 2 years old) |
| | Line of therapy not an inclusion criterion |
| Interventions and comparators: generic/class; specific/drug<br><br>(All interventions will be compared with each other, unless otherwise stated) | Surgery; Gastric bypass<br>Surgery; Gastric band<br>Surgery; Gastric sleeve<br>Surgery; Duodenal switch<br>Endoscopic; Gastric balloon<br>Endoscopic; Duodenal sleeve<br>Diet and exercise; Diet and exercise general<br>Diet and exercise and GRP1 analogues; Diet and exercise and PYY<br>Diet and exercise and GRP1 analogues; Diet and exercise and incretin |
| Outcomes | - % weight change (BMI or kg) at 1 year (Continuous) CRITICAL<br>- Improvement (glycaemic control, i.e. HBA1C) at 1 year (Continuous) CRITICAL<br>- Quality of life at 1 year (Continuous) CRITICAL |

| 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? |
|---|---|
| | - Mortality at 1 year (Dichotomous) IMPORTANT<br>- Weight change (kg) at 1 year (Continuous) IMPORTANT<br>- Remission of T2D at 1 year (Time to event) IMPORTANT<br>- Reduction of diabetic medication (insulin, metformin, SU, TZDs, DP4 inhibitors, GLP1 analogues) (Dichotomous) IMPORTANT |
| Study design | RCT<br>Systematic Review of RCTs |
| Unit of randomisation | Patient |
| Crossover study | Not permitted |
| Minimum duration of study | 1 year |
| Other exclusions | Type 1 diabetes<br>Non-diabetic people<br>Pregnant women<br>Weight loss tablets<br>Duration of type 2 diabetes >10 years<br>Children under 2 years old<br>People of healthy weight |
| Population stratification | 40.0 - 49.9 BMI (kg/m2)<br>35.0 - 39.9 BMI (kg/m2)<br>30.0 - 34.9 BMI (kg/m2)<br>25.0 - 29.9 BMI (kg/m2) |
| Reasons for stratification | Intervention is likely to have a different effect on different BMI thresholds |
| Other stratifications | Type of surgery but they will be combined |
| Sensitivity/other analysis | Combine studies across different types of studies |
| Subgroup analyses if there is heterogeneity | - Sex (All male; All female; Mixed); Expect surgery to work better in women<br><br>- Diabetes treatment (Insulin; No insulin); Expect surgery to work less well in patients treated with insulin<br><br>- Ethnicity (White (>80%); Asian (>80%); Black (>80%)); Expect surgery to have different outcomes in different ethnicities<br>- Medical - Dietician (Diet supervised by dietician; Diet not supervised); Expect surgery to work better in people who have completed supervised diet<br><br>- Medical - VLCD (Very-low-calorie diet; Low-calorie diet); Expect surgery to work better in people who followed a very-low-calorie diet<br><br>- Surgery (Gastric bypass; Gastric band; Gastric sleeve; Duodenal switch); Expect outcomes to be better in people who have undergone surgery<br><br>- Exercise (Physical exercise supervised; Advice on physical exercise); Expect outcomes to be better in people who received supervised physical intervention (than advice alone) |
| Search criteria | Databases: Medline, Embase, the Cochrane Library<br>Date limits for search: None<br>Language: English language only (except studies translated for Cochrane reviews or as directed by the GDG) |

### C.1.3 Follow-up care packages after bariatric surgery

| Review question | What is the clinical and cost effectiveness of follow-up care packages after bariatric surgery compared with usual care? |
|---|---|
| Guideline condition and its definition/method of assessment | Obese and overweight people. Definition – Overweight: 25-29.9 BMI (kg/m2); Obese: >30 BMI (kg/m2) |
| Objectives | To examine the effectiveness of follow-up care packages |
| Review population | Adults and young people (post-puberty) who are overweight and obese |
| Major age categories e.g. adults | As above |
| Line of therapy | Line of therapy not an inclusion criteria |
| Interventions and comparators: generic/class; specific/drug | Follow-up care package that includes:<br>Nutritional monitoring and one of the following:<br>- problems associated with excess weight loss<br>- avoiding weight regain<br>- specialist psychological (behavioural/CBT/Cognitive Analytical Therapy (CAT)), educational, and social support<br>(another term used 'shared-care model of chronic disease management')<br><br>-support for becoming pregnant post-bariatric surgery may also be part of the care package<br><br>(literature on surgical removal of excess skin [body contouring surgery/brachioplasty/abdominoplasty/mastoplexy]will be extracted from data)<br><br>Usual care (defined as nutritional care only – not a package) |
| Outcomes (restrict to 7) | Outcomes<br>% weight loss at end of study (continuous) (in BMI or kg)/% excess weight loss at end of study (continuous) (in BMI or kg) – CRITICAL<br>Development of at least one micronutrient deficiency (i.e. iron, selenium, zinc, vitamin A, calcium, vitamin B12, vitamin B1) – CRITICAL<br>Health related quality of life/Obesity related QOL (IQ QOL, OWL QOL) – CRITICAL<br>Reoperation rate IMPORTANT<br>Mortality (time to event, dichotomous) IMPORTANT<br>Reduction in medication use IMPORTANT<br>Psychological well-being IMPORTANT |
| Study designs | Systematic Reviews of RCTs or RCTs (conference abstracts if no evidence) |
| Unit of randomisation | Patient |
| Crossover study | Not permitted |
| Minimum duration of study | Minimum 1 year, no maximum |
| Other inclusions | None |
| Sample size exclusion criteria | None |
| Other exclusions | Non-English language studies.<br>Abstracts (excluded from the review, not the search). |

| Review question | What is the clinical and cost effectiveness of follow-up care packages after bariatric surgery compared with usual care? |
|---|---|
| Population stratification | Young people – puberty onwards<br>People with learning disabilities |
| Reasons for stratification | Young people are still growing and have different needs after bariatric surgery.<br><br>People with learning difficulties have difficulty with consent and follow-up and may still eat despite having the procedure so are at a higher risk of complications. |
| Other stratifications | None |
| Sensitivity/other analysis | Minimum n=none<br>Data will be meta-analysed if possible<br>Pre-intervention treatment will be considered if reported<br>Minimum length of follow-up = 1 year<br>Time points will be pooled for analysis<br>Continuous outcomes - final values preferred. Change scores and final values will be pooled if required.<br>Time to event outcomes (mortality) will be reported as dichotomous if time to event data not available.<br>Default MIDs will be used unless otherwise stated.<br>If no RCTs for children or young people the GDG will consider extrapolating from adult populations for these groups |
| Subgroup analyses if there is heterogeneity | Type of surgery<br>Male sex, T2D, African-American ethnicity<br>People with renal problems or Type 1 diabetes<br>Women who become pregnant after surgery<br>Housebound patients<br>People on antipsychotic medications or other medications that cause weight gain |
| Search criteria | Databases: Medline, Embase, the Cochrane Library<br>Date limits for search: None<br>Language: restrict to English only<br>Search restrictions: None |

## C.2 Economic evidence reviews

| Review question | All questions – health economic evidence |
|---|---|
| **Objectives** | To identify economic evaluations relevant to the review questions set out above. |
| **Criteria** | • Populations, interventions and comparators must be as specified in the individual review protocols above.<br>• Studies must be of a relevant economic study design (cost–utility analysis, cost–benefit analysis, cost-effectiveness analysis, cost–consequence analysis, comparative cost analysis).<br>• Studies must not be an abstract only, a letter, editorial or commentary, or a review of economic evaluations.[a] Unpublished reports will not be considered unless submitted as part of a call for evidence.<br>• Studies must be in English. |
| **Search** | An economic study search will be undertaken using population-specific terms and an economic |

| | |
|---|---|
| **strategy** | study filter – see Appendix F [in Full Guideline]. |
| **Review strategy** | Each study fulfilling the criteria above will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in Appendix G of the NICE guidelines manual (2012).[1]<br><br>**Inclusion and exclusion criteria**<br>• If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. An economic evidence table will be completed and it will be included in the economic evidence profile.<br>• If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then an economic evidence table will not be completed and it will not be included in the economic evidence profile.<br>• If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.<br><br>**Where there is discretion**<br>The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the GDG if required. The ultimate aim is to include studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the GDG if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation as excluded economic studies in Appendix I.<br><br>The health economist will be guided by the following hierarchies.<br>*Setting:*<br>• UK NHS<br>• OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden)<br>• OECD countries with predominantly private health insurance systems (for example, USA, Switzerland)<br>• non-OECD settings (always 'Not applicable').<br>*Economic study type:*<br>• cost–utility analysis<br>• other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequence analysis)<br>• comparative cost analysis<br>• non-comparative cost analyses including cost-of-illness studies (always 'Not applicable').<br>*Year of analysis:*<br>• The more recent the study, the more applicable it is.<br>• Studies that are based on resource use and unit costs from more than [10] years ago will be downgraded in terms of applicability.<br>*Quality and relevance of effectiveness data used in the economic analysis:*<br>• The more closely the effectiveness data used in the economic analysis matches with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline. |

*(a) Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.*

1 National Institute for Health and Clinical Excellence. The guidelines manual. London: National Institute for Health and Clinical Excellence; 2012. Available from: http://publications.nice.org.uk/the-guidelines-manual-pmg6/