

Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation

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Disclaimer: This report contains transcripts of interviews conducted in the course of the research and contains language that may offend some readers.

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Scientific summary

Surgery, lifestyle interventions, orlistat for severe obesity

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Scientific summary

Background

Adults with severe obesity [body mass index (BMI) of ≥ 35 kg/m²] have an increased risk of comorbidities and psychological, social and economic consequences. Systematic review evidence on the feasibility/acceptability, clinical effectiveness and cost-effectiveness of weight-management programmes (WMPs) for adults with severe obesity is limited.

Aim

The aim of this study was to systematically review the evidence for bariatric surgery, lifestyle WMPs and orlistat for adults with severe obesity, and to evaluate the feasibility, acceptability, clinical effectiveness and cost-effectiveness of treatment.

Methods

We undertook four systematic reviews, which were of:

1. Randomised controlled trials (RCTs) or quasi-randomised trials of bariatric surgery, lifestyle WMPs and orlistat (approved by the National Institute for Health and Care Excellence) with mean or median follow-up durations of ≥ 12 months. We included comparisons between interventions or comparisons with usual care/controls.
2. UK lifestyle WMPs and orlistat with any study design and a mean or median follow-up duration of ≥ 12 months.
3. Qualitative and mixed-methods research on the feasibility and acceptability of lifestyle WMPs and orlistat (including views of professionals involved in care).
4. Economic evaluations (trial analyses and decision modelling studies) of bariatric surgery, lifestyle WMPs and orlistat.

Data from the systematic review of RCTs populated a microsimulation model predicting costs, outcomes and cost-effectiveness of the most-effective programmes over a 30-year time horizon from a NHS perspective for a population representative of all adults with a BMI of ≥ 35 kg/m². The UK Health Forum microsimulation model assessed the cost-effectiveness of:

- the Look AHEAD trial WMP versus baseline UK general population BMI trends
- a very low-calorie diet (VLCD) added to a WMP versus a WMP alone, with both versus the baseline UK general population BMI trend
- Roux-en-Y gastric bypass (RYGB) versus a WMP, with both versus the baseline UK general population BMI trends.

Data sources

Fourteen electronic databases were searched from 1990: MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, PsycINFO, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Science Citation Index, Cochrane Central Register of Controlled Trials (CENTRAL), ClinicalTrials.gov, Social Science Citation Index, CAB Abstracts, NHS Economic Evaluation Database, Health Technology

Assessment (HTA) database, Cost-effectiveness Analysis Registry and Research Papers in Economics (RePEC). The last searches were in May 2017. A total of 1174 reports of RCTs of obesity from prior autoalerts were hand-searched.

Participants

The participants were adults with a mean or median age of ≥ 16 years (≥ 18 years for the systematic review of economic evaluations and microsimulation); there was no upper age limit. All groups of participants in studies had mean or median BMIs of ≥ 35 kg/m².

Setting

All settings for interventions were included (e.g. primary care, secondary care, community, commercial organisations, workplaces, the internet and other digital domains).

Types of outcome measures

The outcomes were weight change (primary outcome), cardiovascular risk factors, psychological well-being, adverse events, quality of life, process outcomes, qualitative outcomes, costs and economic evaluations.

Study appraisal

For each systematic review, one reviewer extracted numerical data from included studies and a second reviewer checked the data. Two reviewers independently carried out quality assessments.

Data synthesis for systematic reviews

For continuous outcomes, mean differences were reported, and for dichotomous outcomes, risk ratios with 95% CIs were reported. Meta-analyses for weight outcomes were analysed taking account and without taking account of dropouts (data presented here). We used random-effects meta-analysis and bivariate mixed-effects metaregression to explore predictors of weight loss. For qualitative data, study design, methods, participants, interventions, findings, data pertaining to area and setting, and quality were extracted and analysed and reported in narrative synthesis. For cost-effectiveness studies, data were narratively synthesised. A realist synthesis approach to integrating the qualitative, quantitative and health economic evidence was undertaken.

Results from randomised controlled trials (systematic review 1)

A total of 131 RCTs were included. Few trials had long follow-up durations, with the exceptions of the US Look AHEAD trial (median duration of 9.6 years and mean weight loss of 6%, in participants with type 2 diabetes mellitus) and two Finnish trials with ≥ 5 years of follow-up. Look AHEAD used a low-fat reducing diet, a calorie goal of 1200–1800 kcal/day, initial meal replacements or meal plans, a tailored exercise programme, cognitive-behavioural therapy (CBT), group and individual support and follow-up by telephone or e-mail.

Bariatric surgery, especially RYGB, produced greater long-term weight change than any of the WMPs [RYGB mean -20.23 kg, 95% confidence interval (CI) -23.75 to -16.71 kg] at 60 months. Adding a VLCD to an

existing WMP gave an additional mean weight change of -4.41 kg (95% CI -5.93 to -2.88 kg) at 12 months. Orlistat and dietary counselling reduced weight regain after VLCDs. Long-term weight maintenance after weight-loss programmes that did not incorporate VLCDs was improved by orlistat and follow-up in person or by telephone.

Data analyses initially favoured low-carbohydrate (< 40 g/day) reducing diets compared with low-fat reducing diets (mean weight change of -1.16 kg, 95% CI -2.13 to -0.19 kg), and higher protein ($\geq 30\%$ energy) reducing diets compared with lower protein reducing diets (mean weight change of -0.91 kg, 95% CI -1.83 to 0.00 kg) at 12 months, but not beyond 12 months. The use of meal replacements, such as giving component parts of VLCDs, was associated with greater weight loss, but only at 12 months (mean weight change of -2.75 kg, 95% CI -4.01 to -1.48 kg).

More intensive interventions, with more contacts with WMP personnel (in person or remotely), were usually associated with greater weight loss and better weight maintenance. Initial inpatient programmes were not associated with greater weight loss. Interventions delivered to groups rather than to individuals had greater weight loss results, but groups usually had more contacts. There was little evidence that incorporating family members for support and modifying the home environment were beneficial. Similarly, interventions that were weight neutral or did not target weight loss were less effective than those with a prescribed calorie content or deficit.

Metaregression analysis of WMPs compared with usual care/control showed that, at 12 and 24 months, the use of VLCDs, providing a prescribed calorie intake or providing a prescribed calorie deficit were important predictors, with a prescribed calorie intake appearing to have more effect than a calorie deficit. Providing an additional in-person physical activity programme to attend or providing orlistat was not a significant predictor of weight loss.

Review of UK studies (systematic review 2)

A total of 26 studies were included: these were mostly non-comparative studies, comprising 10 in primary care, three in primary and secondary care, 11 in secondary care, one in a commercial setting and one in a community setting. Seven were in specialist weight-management services. Only nine studies had follow-up durations of > 12 months. Limitations in denominators, and differences in participant groups, made comparisons challenging.

Very low-calorie diets showed a mean weight change of -12.4 kg [standard deviation (SD) 11.4 kg] to -15.0 kg (SD 9.6 kg) at 12 months, with dropouts up to 25.3%, but unclear weight loss after 12 months of the programme. One specialist weight-management service showed a mean weight change of -5.9 kg (SD 10.7 kg) at 24 months for people who completed 12 months. Under one-third of UK studies reported incorporating group sessions, which qualitative research showed that participants favoured and which systematic review 1 showed produced better weight loss.

Review of qualitative studies (systematic review 3)

A total of 33 studies were included. Participants described being attracted to programmes perceived to be novel or exciting in some key way, which had been endorsed by their health-care provider (a view supported by programme providers). The sense of belonging to a group who shared similar issues relating to weight and food and who had similar physiques and personalities was particularly important. This seemed to foster a strong group identity and accountability, which seemed to help motivation and continuing engagement. However, some participants described struggling with physical activity programmes (owing to physical comorbidities) and not everyone enjoyed group interactions (sometimes owing to mental health comorbidities).

Review of cost-effectiveness (systematic review 4)

A total of 46 studies were included. Many evaluations were of short duration or did not include extrapolations of input data, failing to fully capture long-term implications of obesity-related disease. Modelling assumptions regarding weight regain after the period of weight loss were poorly described, and their impact on long-term cost-effectiveness was rarely tested in sensitivity analyses. There was a lack of high-quality long-term data on the cost-effectiveness of VLCDs in a UK setting. Data on the cost-effectiveness of orlistat showed mixed results. When compared with WMPs, surgery was cost-effective. When compared with no treatment, surgery was sometimes cost saving, with the savings from reduced obesity-related comorbidities offsetting surgery costs. However, the cost-effectiveness of surgery depended on the quality of model input data, which were rarely of sufficient quality to fully capture the costs of preparation, delivery, complications and, most importantly, long-term follow-up after bariatric surgery. None of the studies included any quality-of-life decrements for surgery-related complications, which might overstate the cost-effectiveness of surgery.

Economic model

Weight-management programmes were generally cost-effective compared with a baseline of current UK general population obesity trends [incremental cost-effectiveness ratio < £20,000/quality-adjusted life-year (QALY)]. However, the addition of a VLCD to a WMP was not cost-effective. The Look AHEAD programme was borderline cost-effective compared with current population obesity trends, with an improved case for cost-effectiveness under longer-term weight regain assumptions. RYGB was the most cost-effective strategy overall in the base-case analysis, over a 30-year time horizon, although the model did not replicate long-term cost savings for surgery suggested by some studies in systematic review 4. The economic model results were sensitive to assumptions about weight regain, model time horizon and discount rates for costs and QALYs.

Strengths and limitations

Reviewed studies often lacked generalisability to the UK setting in terms of participants' characteristics, such as very high BMI scores and socioeconomic disadvantage, and available resources for implementation. Studies often excluded people with eating disorders or problems with mental health or addiction. Studies usually lacked long-term follow-up (particularly complications from surgery), leading to unrealistic weight regain assumptions. The views of potential and actual users of services were rarely reported to contribute to service design. Economic evaluations were often limited by a lack of data, particularly for weight regain after weight loss. Despite rigorous searching, we may particularly have failed to identify unpublished UK evaluations. Dual, blinded numerical data extraction was not undertaken. The results should, therefore, be interpreted with caution.

Implications for health care

1. Roux-en-Y gastric bypass surgery was the most cost-effective weight-loss strategy, favoured over lifestyle WMPs and current population obesity trends. However, shorter time horizons and higher discount rates reduced the cost-effectiveness of bariatric surgery and RYGB might not then be the most cost-effective use of resources. In such cases, a less intensive lifestyle WMP might be a short-term cost-effective alternative. However, shorter time horizons may be insufficient to capture all of the relevant long-term benefits and cost savings of the obesity-related diseases avoided as a result of surgery.
2. In systematic review 4, bariatric surgery tended to be more cost-effective in younger people and people without comorbidities. However, there were no comparable subgroup analyses in studies evaluating lifestyle WMPs.

3. Adding a VLCD to a WMP was not cost-effective; however, a VLCD with a WMP was cost-effective compared with current population trends. Furthermore, VLCDs might reduce the number of dropouts and increase motivation.
4. The Look AHEAD intervention was borderline cost-effective in our base-case analysis. It is more likely to be cost-effective extrapolating slower linear weight regain after 9 years of the programme.
5. In primary care, the standard Counterweight Programme was effective at producing weight loss, and adding a VLCD to this produced greater weight loss at 12 months. Weight loss in the standard Counterweight Programme was comparable with that in the remotely delivered Positive Online Weight Reduction (POWeR+) programme, which recruited from general practice.
6. Diets with low-carbohydrate (< 40 g/day) or higher protein content ($\geq 30\%$ energy) or with the addition of meal replacements led to slightly greater weight loss at 12 months only. Adding an additional intensive physical activity programme to attend provided longer-term and greater weight-loss increments than these dietary changes. Whether or not less intensive physical activity programmes, as opposed to physical activity advice, have this effect was unclear. Physical activity programmes may be of particular interest to men.
7. Prescribing orlistat and continuing telephone or in-person contact for people following a WMP or weight maintenance led to additional weight loss over the WMP alone.
8. Adding additional telephone or internet support, and group support, to a standard WMP was more effective than the WMP alone. There was weaker evidence to support CBT, motivational interviewing and mindfulness.
9. Weight-management programmes that were perceived to be novel or exciting and endorsed by health-care providers tended to be valued.
10. Group-based programme activities tended to be valued along with fairly intensive support from programme providers.
11. Weight-neutral interventions, without a focus on a calorie content or reduction, did not appear to be helpful for weight loss.

Recommendations for research

Quantitative research

1. Randomised controlled trials should report in greater detail items needed to assess risk of bias, equity, coding for behaviour change techniques and fidelity data.
2. The provision of protocols and WMP materials would contribute to the evidence base for improving the design of WMPs.
3. Randomised controlled trials should have adequate statistical power and attempt much longer follow-up durations than 1 year for weight, comorbidities, quality of life and adverse events; ideally, follow-up durations should be ≥ 5 years.
4. Hard-to-reach or disadvantaged groups, younger or older adults and people with very high BMI scores were inadequately represented in the evidence. These groups should be a focus of research.
5. Randomised controlled trials and economic evaluations should examine different approaches to weight management for people eligible for Tier 3 weight-loss services, particularly regarding whether or not VLCDs should be routinely offered or whether or not NHS Tier 3 services provide better outcomes than commercial programmes.
6. Long-term UK weight outcome data (including dropouts), using a standard evaluation framework, are needed from commercial providers for participants with severe obesity.
7. Randomised controlled trials comparing calorie-prescribed diets versus diets with a prescribed deficit should examine if the former are easier to prescribe and adhere to and more effective for weight loss.

Qualitative and mixed-methods research

There is a lack of published qualitative research on the views of potential users, participants, 'low users', people who drop out and providers of WMPs for people with severe obesity, including, but not limited to, Tier 3 services in the UK. Better descriptions of patient characteristics would help further analyses. Programmes should involve potential participants in the design and development of services.

Recommendations for analysis and reporting of economic models of weight-management programmes

1. Improved description and justification of key model inputs, such as cost inputs and utility weights.
2. Include all relevant costs, including all preoperative and postoperative costs, long-term follow-up after bariatric surgery and the cost of long-term complications.
3. Transparent presentation of assumptions in health economic models, particularly long-term weight regain assumptions, preferentially based on actual data.
4. Decision models should include important disease health states sufficient to give a true picture of chronic obesity.
5. Clearly identify long-term effectiveness of VLCDs using long-term weight outcome data derived from RCTs.

Study registration

This study is registered as PROSPERO CRD42016040190.

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