Section 6: Health economics

The following section includes two separate pieces of work on the cost effectiveness of interventions in clinical and public health settings. The literature review for both pieces of work identified a paucity of data on the cost effectiveness of interventions, particularly interventions undertaken in the UK and with more than 1-year follow-up. As a result, additional economic modelling was undertaken.

Although the health economic reviews and analyses were carried out by two different teams; both followed NICE methodologies, as set out in the Guidelines Development Methods manual, and liaised closely on the parameters used in their analyses, such as on diseases to include and QALY scores, so that both the clinical and public health work were consistent and complementary.

16 Cost effectiveness of clinical interventions

16.1 Introduction

Although the management of obesity in itself is potentially beneficial to the quality of life (QoL) of people, the role of obesity management is integral to the management of numerous further conditions. These include (among many others) myocardial infarction,[1] coronary heart disease, stroke and atrial fibrillation,[2] stress incontinence, diabetes, dyslipidaemia, back pain and arthritis.[3] The economic burden of this is increasing as obesity levels rise in England and Wales. Data from the 'Health survey for England' indicated that, in 2001, the prevalence of obesity had reached 21% in males and 23.5% in females. This has cost implications for both the healthcare system and the broader community.

Recent evidence has suggested that, after adjustment for age, sex, deprivation category, country and the presence of a comorbidity, people with a body mass index (BMI) greater than 30 kg/m^2 receive more prescriptions than those with a BMI between 18.5 kg/m^2 and 25 kg/m^2 focusing on prescriptions aimed at tackling problems in the following areas: the cardiovascular system, the central nervous system, the endocrine system, musculoskeletal and joint problems, infections, gastrointestinal problems and skin problems (all p values less than 0.05).[4] Furthermore, evidence from the UK suggests that there is a significantly higher level of medical contacts among the obese than among those of a healthy weight (general practitioner [GP], practice nurse or hospital outpatient attendance [all p values less than 0.001], and hospital inpatient attendance [p = 0.034]).

From a broader perspective, it is important to note that the burden of obesity also falls outside the healthcare sector. National Audit Office figures suggest that the burden on society is approximately £2 billion, significantly higher than the medical burden of £479.4 million spent on treating obesity per se and all obesity-related conditions. This £2 billion figure covers the loss in productivity of the UK economy due to obesity. Furthermore, there are costs to patients and carers of obesity and its effects. Although this area is not explicitly addressed in this discussion, it is potentially a significant factor in the study of the topic. Any recommendation designed to reduce the level and severity of obesity (or prevent weight gain) based

on cost-effectiveness evidence must balance the costs of the intervention against the expected benefit to the individual. This cost implication must account not only for the cost of intervention but also the reduced spending on the management of obesity and all related conditions.

The objective of this work was to assess the cost effectiveness of strategies involved in the management of obese individuals.

16.2 Methods

16.2.1 Research questions

There was no good-quality cost-effectiveness evidence on the identification or assessment of obesity. Therefore, the Guidance Development Group decided to focus on treatment options for people with differing degrees of obesity.

16.2.1.1 Major question

- What is the cost effectiveness of interventions used in the clinical management of obesity?

16.2.1.2 Sub questions

- What is the cost effectiveness of non-pharmacological interventions in the clinical management of obesity?
- What is the cost-effectiveness of orlistat in the clinical management of obesity?
- What is the optimal treatment length in the use of orlistat?
- What is the cost effectiveness of sibutramine in the clinical management of obesity?
- What hurdles should be used in the protocol for sibutramine?
- What is the cost effectiveness of surgery in the clinical management of obesity?
- To what extent are all of these discussions generalisable to children?

16.2.2 Data sources and search strategies

The following information sources were searched:

- Medline
- EMBASE
- Cumulative Index to Nursing and Allied Health Literature (Cinahl)
- PsycINFO
- NHS Economic Evaluation Database (NHS EED)

The electronic search strategies were developed in Medline and adapted for use with the other information sources. A search of titles and abstracts was undertaken and full papers were obtained if they appeared to address the Guidance Development Group's (GDG's) question relevant to the topic. No criteria for study design were imposed a priori. In this way the searches were not constrained to randomised controlled trials (RCTs) containing formal economic evaluations. Papers included were:

- limited to studies with a study population of BMI greater than 27 kg/m^2
- written in English, and reported health economic information that could be generalised to the UK.

The full papers were critically appraisal by a health economist using a standard validated checklist. A general descriptive overview of the studies, their qualities, and conclusions was presented and summarised in the form of a narrative review. Any further work was negotiated in partnership with the GDG, targeting areas with the most uncertainty and/or the greatest capacity for improving health outcomes.

16.3 Cost effectiveness of non-pharmacological interventions

16.3.1 Cost effectiveness statements for non-pharmacological interventions (Table 16.1)

Table 16.1 Cost effectiveness statements

1	There is little evidence specifically on the cost effectiveness of non-pharmacological interventions (diet, physical activity and behavioural treatment) in the treatment of obesity
2	The degree of cost effectiveness of non-pharmacological interventions is highly sensitive to the duration of benefit
3	If weight loss relative to trend remains constant for 5 years post-intervention before returning to baseline, the cost per QALY in the best-performing non-pharmacological studies ranges from £174 to £9971

QALY, quality-adjusted life year.

16.3.2 Approach

In this section, the analysis contains two tributary components. First, there is a full literature search, looking for health economics papers reporting interventions in a population with BMI greater than 28 kg/m^2. Second, the clinical papers selected for this review (but containing little economic evidence) are investigated, looking at the relation between intensity and type of intervention and outcome.

16.3.3 Literature search

The search yielded four papers dealing with the cost effectiveness of non-pharmacological interventions, three of which dealt with interventions primarily in adults and one dealing with families. These are appraised below. Due to the relatively low quality and generalisability of these papers, a further pharmacological paper was identified that provided further useful information.

16.3.3.1 Non-pharmacological interventions in adults

A study conducted in Australia looked at the cost effectiveness of nutrition counselling in general practice (Table 16.2).[5] The researchers employed two treatment arms and a control group, with 273 patients randomly assigned to one of two intervention groups (doctor and dietitian or dietitian alone). Both of the intervention groups received six counselling sessions over 12 months from the

dietitian. In the doctor and dietitian arm, it was the doctor who invited the patient to join the study and to review progress at two of the six sessions. Further details of the intervention are given in Section 5.

Table 16.2 Results of Pritchard and co-workers'' study on cost effectiveness of nutrition counselling in general practice[5]

	Group		
(All costs in Aus$)	**Control**	**Doctor/dietitian**	**Dietitian**
Total cost per group	2103.53	8240.30	5715.06
No. of patients	91	93	89
Cost per patient	23.12	88.61	64.21
Additional cost per patient	–	65.49	41.09
Weight change per patient (kg)	0.58	–6.13	–5.05
Additional weight change per patient (kg)	–	–6.71	–5.63
Additional cost per kg lost	–	9.76	7.30

If these tabulated results are reliable, the cost per kg lost is highly indicative of cost effectiveness of the interventions relative to the control. At October 2005 exchange rates, the incremental cost per kilogram lost is £4.13 and £3.09 for the doctor/dietitian and dietitian groups, respectively.

An American study reviewed the literature on the cost effectiveness of nutrition services.[6] It searched for economic papers published between January 1966 and September 2001 and found 13 studies. Two studies had both an obese population and weight loss as a study outcome,[5,7] one of which did not appear in the guidance literature search results.

A small American study looked at the cost effectiveness of a television-delivered behavioural weight loss programme.[7] A total of 77 patients were randomised to one of four groups: a live-contact group that was videotaped; a live-contact group that was not videotaped; a television-delivered group that observed the videotaped weight loss sessions; and a waiting-list control group. All three treatment groups lost significantly more weight and decreased their percentage of overweight significantly more than the control (Table 16.3). However, the differences between the treatment groups were not statistically significant.

Table 16.3 Results of Meyers and co-workers'' study on cost effectiveness of a television-delivered behavioural weight loss programme[7]

Group and time	Mean ± SD body weight (kg)	Mean ± SD % overweight
Videotaped		
Pre-treatment	82.06 ± 17.87	36.5 ± 22.2
Post-treatment	77.93 ± 13.90	29.8 ± 23.3
Television delivered		
Pre-treatment	88.77 ± 10.66	42.4 ± 17.0
Post-treatment	84.55 ± 10.02	35.6 ± 16.8
Live contact		
Pre-treatment	86.55 ± 15.69	44.2 ± 25.5
Post-treatment	82.06 ± 15.65	36.8 ± 25.4
Waiting-list control		
Pre-treatment	91.72 ± 23.27	40.0 ± 24.4
Post-treatment	90.86 ± 23.63	38.9 ± 25.8

The authors suggested they collected cost data but did not report it in the article. However, their conclusion was that, since the television-delivered care used significantly fewer resources than the similarly successful live contact groups, the television medium should be considered as a cost-effective intervention.

16.3.3.2 Non-pharmacological interventions in adolescents

An American study looked at the cost effectiveness of group and mixed family-based treatment for childhood obesity.[8] Thirty-one families with obese children (child between 20% and 100% overweight, neither parent greater than 100% overweight, one parent willing to attend treatment meetings, no family member participating in an alternative weight control programme, no child or parent having current psychiatric problems, and no dietary or exercise restrictions on the participating parent or child) were randomised to groups with either both group and individualised treatment or group treatment alone.

Group treatment involved eight weekly meetings, followed by four bi-weekly meetings and one monthly meeting. Each group intervention contained 12 adults and 12 children, with the adults and children being seen separately. A mastery approach

to teaching was used to inform families how to alter eating habits. Course material was tailored to the age of the individual. Content included diet, activity, behaviour change techniques, parenting and coping with psychosocial problems experienced by obese children.

Patients in the mixed treatment arm received 15–20-minute individual sessions parallel to the group sessions. Individual therapy was designed to help participants identify weight-affecting behaviour, to determine the accuracy of habit book recording, to evaluate the progress towards goals and to provide performance feedback. The costs per family for the mixed and group-only approaches were US$1390.72 and US$491.48, respectively.

The group treatment was associated with a larger decrease in percentage overweight ($p < 0.05$) and in z-BMI ($p < 0.01$) per dollar spent. At 12 months, a decrease of 0.5% overweight units per US$100 was observed in the mixed treatment branch compared with a 1.4% decrease in the group-only branch. Thus, the mixed therapy provided a lower reduction in weight at a higher cost than group therapy. This paper looked at moderately obese families. The authors noted that, although it was not cost effective to provide individual therapy to this group, it may be cost effective to do so for the more obese population. A further consideration may be the effect of reduced weight on future costs. This is likely to reduce the overall cost burden to the system and make both interventions more cost effective relative to doing nothing.

16.3.3.3 Control branches in pharmacological trials

One study included diet and exercise advice as the control.[9] In this evaluation, monitoring was performed by the GP for the first year (monthly visits each costing £13), and by a nurse for the second year (monthly visits each costing £7.29). Beyond this time, the assumptions used in the model meant that the patients had returned to baseline. Thus, no further costs were accrued beyond year 2. The cost for this is therefore £243.48 per person.

In terms of weight loss, the paper suggested that the placebo group was never more than 3 kg lighter than the trend weight group (who gained weight at 1 kg per year)

and returned to trend in 18 months. The precise weight pathway is not provided. A reduction of 2 kg over 18 months followed by a return to baseline in 6 months was inputted into the guidance economic modelling (described in depth in section 16.5.4.). This modelling includes the effect of weight loss on QoL, diabetes and mortality. This led to an increase of 0.015 quality-adjusted life years (QALYs) in men and 0.014 QALYs in women. Using the cost provided of £243.48, this implies a cost per QALY of £16,232 for men and £17,391 for women.

These values are likely to underestimate cost effectiveness of the intervention for three major reasons. First, the modelling uses a simplifying assumption of limiting benefit to reduction in prevalence of coronary heart disease (CHD), type 2 diabetes and colorectal cancer. Second, the protocol for non-pharmacological care given in the economic evaluation is intensive. If the same (or similar) results can be gained using fewer than the 24 visits suggested by Warren and co-workers', the cost per QALY will fall further. Finally, the benefit of weight loss through non-pharmacological interventions is likely to continue beyond the intervention period. Indeed, it can be argued that a successful non-pharmacological therapy elicits a change in behaviour that lasts for a lifetime. If this is the case, the cost per QALY will fall.

16.3.3.4 Investigating the search results for clinical papers

The clinical review looked at three major areas of non-pharmacological interventions, specifically behavioural treatment, diet and exercise. Since this economics review is investigating the incremental benefit of particular interventions, the clinical reviews were filtered to look at those interventions for which the difference between the intervention and the control was only one approach. Thus, for example, diet versus no intervention was included, as was diet and exercise versus exercise alone. Furthermore, the papers included here had to report sufficient detail regarding the quantity of contact time and the healthcare professional involved. Also, the paper needed to present results at 12 months. For the purpose of the analysis, it is assumed that each intervention continues for this period before being discontinued. The reviews included papers that met these specifications as shown in Table 16.4.

Table 16.4 The number of clinical papers included by intervention[a]

Review	Diet	Behavioural treatment	Physical activity
No. of papers included in review	6	1	2

[a] Many of the studies published in these areas involve components of two or three or these types of intervention. The physical activity review looks for any paper that includes physical activity, the behavioural treatment review looks at papers that combine behaviour therapy with diet, and the diet review looked at papers which include diet alone (thus only those papers in which the control is no intervention).

The aim of this section is to balance the resource implications of these programmes against the benefit to the patients. Effectiveness data for the papers taken from the physical activity review (Table 16.5) are given here.

Table 16.5 The relevant effectiveness papers in the physical activity review

Author(s)	Comparison	Additional Intervention in first year	Relative weight loss at 12 months (kg)
Anderssen SA, Hjermann I, Urdal P et al. Improved carbohydrate metabolism after physical training and dietary intervention in individuals with the 'atherothrombogenic syndrome'. Oslo Diet and Exercise Study (ODES). A randomized trial. *Journal of Internal Medicine* 1996;240:203–9	Physical activity vs no treatment	158 sessions of up to 1 hour by a 'highly qualified instructor' (assumption of physiotherapist taking groups of six)	2.00
Pritchard JE, Nowson CA, Wark JD. A worksite program for overweight middle-aged men achieves lesser weight loss with exercise than with dietary change. *Journal of the American Dietetic Association* 1997;97:37–42	Physical activity vs no treatment	19 compulsory contacts by an unreported healthcare professional (assumption of physiotherapist and 1-hour contacts)	2.90

Similarly, effectiveness data for the papers taken from the diet review (Table 16.6) are given here.

Table 16.6 The relevant effectiveness papers in the diet review

Authors	Comparison	Additional intervention in first year	Relative weight loss at 12 months (kg)
Frey-Hewitt B, Vranizan KM, Dreon DM et al. The effect of weight loss by dieting or exercise on resting metabolic rate in overweight men. *International Journal of Obesity* 1990;14:327–34	600 kcal/day or low fat vs no treatment	23 extra contacts by dietitian (assumption of 1 hour)	7.06
Jones DW, Miller ME, Wofford MRL et al. The effect of weight loss intervention on antihypertensive medication requirements in the hypertension Optimal Treatment (HOT) study. *American Journal of Hypertension* 1999;12:1175–80	600 kcal/day or low fat vs no treatment	18 extra dietitian contacts (assumption of 1 hour)	0.40
Anderssen SA, Hjermann I, Urdal P et al. Improved carbohydrate metabolism after physical training and dietary intervention in individuals with the 'atherothrombogenic syndrome'. Oslo Diet and Exercise Study (ODES). A randomized trial. *Journal of Internal Medicine* 1996;240:203–9	600 kcal/day or low fat vs no treatment	4 consultations with dietitian (assumption of 1 hour)	5.10
Pritchard DA, Hyndman J, Taba F. Nutritional counselling in general practice: a cost effective analysis. Journal of Epidemiology and Community Health 1999;53:311–16	600 kcal/day or low fat vs no treatment	5 contacts by dietitian (assumption of 1 hour)	5.70
Wood PD, Stefanick ML, Williams PT et al. The effects on plasma lipoproteins of a prudent weight-reducing diet, with or without exercise, in overweight men and women. *New England Journal of Medicine* 1991;325:461–6	600 kcal/day or low fat vs no treatment	23 group sessions with dietitian (assumption of 1 hour and a group of six)	6.10

Authors	Comparison	Additional intervention in first year	Relative weight loss at 12 months (kg)
Stenius-Aarniala B, Poussa T, Kvarnstrom J et al. Immediate and long term effects of weight reduction in obese people with asthma: randomised controlled study. *BMJ* 2000;320:827–32	Very-low-calorie diet vs no treatment	No extra intervention (contact time in control used to discuss themes chosen by participants)	13.40

Finally, the effectiveness results for the relevant behavioural treatment papers are given in Table 16.7.

Table 16.7 The relevant effectiveness papers in the behavioural treatment review

Authors	Comparison	Additional Intervention in first year	Relative weight loss at 12 months (kg)
Wadden TA, Sternberg JA, Letizia KA et al. Treatment of obesity by very low calorie diet, behavior therapy, and their combination: a five-year perspective. *International Journal of Obesity* 1989;13 (Suppl. 2):39–46	Diet and behavioural treatment vs diet	14 extra contacts. 90 minute contacts with clinical psychologist	8.19

This information has to be compared with the costs of the staffing resources (which are likely to represent the majority of the total cost; Table 16.8) used in each intervention group relative to each control group (Tables 16.9–16.11).

Table 16.8 Unit costs of various healthcare professionals[10]

Resource per hour	Unit cost (per hour)
Dietitian	£27
Physiotherapist	£28
Clinical psychologist	£32

Table 16.9 The cost, the effect and the cost per kg lost in physical activity papers

Authors	Relative weight loss at 12 months (kg)	Intervention cost per patient (£)	Cost per kg lost (£)
Anderssen SA, Hjermann I, Urdal P et al. Improved carbohydrate metabolism after physical training and dietary intervention in individuals with the 'atherothrombogenic syndrome'. Oslo Diet and Exercise Study (ODES). A randomized trial. *Journal of Internal Medicine* 1996;240:203–9	2.00	737	368.50
Pritchard JE, Nowson CA, Wark JD. A worksite program for overweight middle-aged men achieves lesser weight loss with exercise than with dietary change [see comment]. *Journal of the American Dietetic Association* 1997;97:37–42.	2.90	532	183.45

Table 16.10 The cost, the effect and the cost per kg lost in diet papers

Authors	Relative weight loss at 12 months (kg)	Intervention cost per patient (£)	Cost per kg lost (£)
Frey-Hewitt B, Vranizan KM, Dreon DM et al. The effect of weight loss by dieting or exercise on resting metabolic rate in overweight men. *International Journal of Obesity* 1990;14:327–34	7.06	621	87.96

Authors	Relative weight loss at 12 months (kg)	Intervention cost per patient (£)	Cost per kg lost (£)
Jones DW, Miller ME, Wofford MRL et al. The effect of weight loss intervention on antihypertensive medication requirements in the hypertension Optimal Treatment (HOT) study. *American Journal of Hypertension* 1999;12:1175–80	0.40	486	1215.00
Anderssen SA, Hjermann I, Urdal P et al. Improved carbohydrate metabolism after physical training and dietary intervention in individuals with the 'atherothrombogenic syndrome'. Oslo Diet and Exercise Study (ODES). A randomized trial. *Journal of Internal Medicine* 1996;240:203–9.	5.10	108	21.18
Pritchard DA, Hyndman J, Taba F. Nutritional counselling in general practice: a cost effective analysis. *Journal of Epidemiology and Community Health* 1999;53:311–16	5.70	135	23.68
Wood PD, Stefanick ML, Williams PT et al. The effects on plasma lipoproteins of a prudent weight-reducing diet, with or without exercise, in overweight men and women. *New England Journal of Medicine* 1991;325:461–6	6.10	103.5	16.97
Stenius-Aarniala B, Poussa T, Kvarnstrom J et al. Immediate and long term effects of weight reduction in obese people with asthma: randomised controlled study. *BMJ* 2000;320:827–32	13.40	0	N/A

N/A, not applicable.

Table 16.11 The cost, the effect and the cost per kg lost in behavioural treatment papers

Authors	Relative weight loss at 12 months (kg)	Intervention cost per patient (£)	Cost per kg lost (£)
Wadden TA, Sternberg JA, Letizia KA et al. Treatment of obesity by very low calorie diet, behavior therapy, and their combination: a five-year perspective. *International Journal of Obesity* 1989;13 (Suppl. 2):39–46	8.19	672	82.05

The final question is whether this information suggests the programmes listed above represent a cost-effective use of societal resources, assuming the individual will return to trend. Since there is great heterogeneity of intervention, it is assumed that the study producing the best cost per kg lost represents 'best practice'. The most important assumption is the rate at which the individual returns to trend weight. To illustrate the importance of this, an alternative scenario is presented in Table 16.12.

Table 16.12 The two scenarios to investigate the sensitivity of the modelling to weight regain assumptions

Scenario	Trend weight gain per annum (kg)	Weight gain post-treatment per annum (kg)	Period before weight returns to trend
Base case	0.5	5.6	Dependent on initial weight loss
Scenario 2	0.5	0.5	5 years

Bearing in mind the small sample of papers amenable to this analysis, the results are suggestive of cost effectiveness in these interventions. Using the papers that report the best cost-effectiveness outcomes (thus representing the 'best practice' in the area), the weight loss was inputted into the economic modelling developed for this guidance and is described in the depth in section 16.5 (on orlistat), generating the QALY gain, aggregate costs and incremental cost-effectiveness ratios (ICER) as shown in Tables 16.13 and 16.14.

Table 16.13 Base case results

Intervention	Incremental cost	Incremental QALY	ICER (£)
Diet (Wood et al. 1991)[11]	75.83	0.0371882	2,039
Behavioural treatment (Wadden et al. 1989)[12]	626.13	0.058361	10,729
Exercise (Pritchard et al. 1997)[13]	523.45	0.0127209	41,149

See Tables 16.7, 16.9 and 16.10 for full publication details of the papers.

Table 16.14 Scenario 2 results

Intervention	Incremental cost	Incremental QALY	ICER (£)
Diet (Wood et al. 1991)[11]	16.92	0.0974152	174
Behavioural treatment (Wadden et al. 1989)[12]	554.44	0.1271699	4,360
Exercise (Pritchard et al. 1997)[13]	491.74	0.049318	9,971

See Tables 16.7, 16.9 and 16.10 for full publication details of the papers.

Since these interventions are applicable to similar population groups, incremental analysis can be used to compare options. As the exercise option is both more expensive and less effective (in terms of 12-month weight loss) than the diet option in both scenarios, it is removed from the analysis since it is dominated. The incremental QALY of behavioural treatment relative to diet can be calculated for both scenarios. Under the base case, the ICER is £25,991, suggesting that the cost effectiveness of the more intensive intervention is unproven. Under scenario 2, the equivalent value is £18,065, representing weak evidence of cost effectiveness of behavioural treatment relative to diet. The important point is that, as the duration of weight loss increases, intensive interventions becomes relatively more cost effective as the benefits endure. It should be noted that, since the guidance is aiming at a multifaceted approach to non-pharmacological care, the trade-off between options becomes less important.

16.3.3.5 Conclusions on the cost effectiveness of non-pharmacological interventions

Notwithstanding the limited evidence in an already obese population, these types of interventions appear to be a cost-effective use of resources. Dietary interventions seem particularly cost effective due to the low levels of staff contact needed. These results seem to agree with the analysis undertaken in the prevention component of the guidance as well as what evidence could be found in the literature search.

A number of caveats must be attached to using these results as unequivocal evidence of cost effectiveness of these kinds of interventions. First, the results are particularly sensitive to the rate of weight regain after the intervention. Thus, cost effectiveness depends on the intervention changing behaviour for a time after treatment is discontinued. Second, since the trials used did not collect cost-effectiveness evidence specifically, the costs of the interventions are only approximate, and contain only staffing costs which, although forming the majority of the cost, exclude some other components. Third, the pool of suitable information is small, and the papers contained slightly different populations. Therefore, the generalisability of the results is questionable. Because of these reasons, these results should be treated as corroborative evidence, rather than definite proof of the cost effectiveness of non-pharmacological interventions.

16.4 Cost effectiveness of sibutramine

16.4.1 Cost effectiveness evidence statements (Table 16.15)

Table 16.15 Evidence statements on cost effectiveness of sibutramine

1	Sibutramine is a cost-effective intervention in adults with a BMI greater than 30 kg/m^2 (or 28 kg/m^2 with comorbidities) relative to non-pharmacological interventions
2	The most reliable estimate of a cost per QALY under current licensing is £6 349 (range: £4 542 – 12 227)
3	There is no evidence regarding the cost-effectiveness of a longer regimen (> 12 months) of sibutramine relative to a regimen of 12 months
4	There is no evidence regarding the cost effectiveness of sibutramine in children and adolescents

16.4.2 Current report – summary and analysis

Consideration of: **O'Meara S, Riemsma R, Shirran L et al. The clinical effectiveness and cost-effectiveness of sibutramine in the management of obesity: a technology appraisal. *Health Technology Assessment* 2002;6:1–97.[14]**

This report was commissioned to provide evidence to the NICE Appraisals Committee. This report undertook a comprehensive literature study and found no cost-effectiveness evidence of a satisfactory standard. It then discussed the previous company (Abbott) submission, submitted as part of the HTA process (BASF Pharma/Knoll. Cost-utility analysis of sibutramine. Submission to NICE.).

The hypothetical population used in their model included 1000 patients with a BMI greater than 30 kg/m^2 who were free of comorbidities and complications at the beginning of the modelling period. Each individual simulated by the model received sibutramine according to the product monograph. A description of the sibutramine regimen is given below:

- 'Hurdle 1 (H1): 2 kg must be lost after 4 weeks of treatment
- Hurdle 2 (H2): 5% of initial body weight must be lost by 12 weeks of treatment

- Hurdle 2a (H2a): In patients in whom either hurdle fails can be given a higher 15 mg dosage for 3 months. Five per cent of initial weight must be lost during this 3-month period.'

The authors used published literature on the effectiveness of sibutramine, (Knoll. Report number SB1047 (Smith 1994). Submission to NICE; Knoll Report number SB1048 (James, 1999)) diabetes risk[15–16] and QoL gains through sibutramine-induced weight loss.[17,18] They used these clinical data to produce overall measurements of total costs and total benefit in terms of mortality and morbidity. The submission suggests a cost per QALY of £10,500 for sibutramine treatment in comparison with a diet and exercise regimen alone. This figure includes the reductions in CHD, diabetes and weight per se and would usually be considered cost effective. The submission asserted that including other beneficial reductions in disease incidence would reduce this cost per QALY further. The Health Technology Assessment (HTA) report noted that the side effects of sibutramine treatment were excluded from the analysis. Under univariate analysis, these results were relatively robust to the assumptions used, in that the cost per QALY range was £3,200 to £16,700.

The HTA looked at areas in the model such as the rate of natural weight regain, regain after treatment has been discontinued. They felt that 'a more realistic cost per QALY gained may be of the order of £15,000 to £30,000'.

16.4.3 Literature search

The update literature review looked for cost-effectiveness studies produced since the cut-off point of the HTA report (June 2000). It identified two studies looking at the use of sibutramine treatment for obesity. They were cost–utility or cost–effectiveness analyses, based in developed countries and had sibutramine as part of the treatment branch. Both were limited to the use of sibutramine in the treatment of obesity in adults.

Since there were no cost-effectiveness studies on the use of sibutramine in children and adolescents, the clinical review on the effectiveness in this area was used in

conjunction with the adult cost-effectiveness review to provide guidance on the formulation of recommendations in this group.

A company submission looked at the cost effectiveness of treating obese people with sibutramine [19] and a diet and exercise regimen relative to the 'best non-pharmacological care', comprising a diet and exercise regimen alone. Patients were treated in accordance with the product monograph given previously. Commencing treatment on a daily dose of 10 mg, patients must pass the hurdles to remain in the treatment group.

Effectiveness data comprise weight loss progress over the treatment year, weight regain after the year,[20,21] reduction in (and improvement in QoL associated with) CHD[22]–[23] and diabetes,[24],[25] and QoL life gains through weight loss per se.[26,27] Side effects were not explicitly discussed. The most severe side effects would be partially contained in the dropout rates assumed in the model.

Cost data comprised of costs accrued through following the sibutramine treatment recommendations of the Nutrition Committee of the Royal College of Physicians,[28] the costs of CHD events sourced from the United Kingdom Prospective Diabetes Study (UKPDS) study,[29] and the costs of diabetes treatment taken from a number of sources including the UKPDS. The perspective selected that of the UK NHS and personal social services. Therefore, no calculation of issues such as productivity losses or costs incurred to patients is included. This step follows the approach of the Institute's technical manual. The paper discounts future events at 6% for costs and 1.5% for benefits. This differs from the Institute's current approach of discounting both costs and benefits at 3.5% (although it does follow previous NICE recommendations, used until recently). The effect of this difference is to marginally underestimate the true cost per QALY of the treatment arm relative to the control. The timescale is the lifetime of the person following the maximum treatment period of 12 months. The specific population considered had a BMI of at least 30 kg/m^2 without comorbidities. The population was 80% female, reflecting UK prescription data.

The results were as follows:

- The use of sibutramine in the cohort of 1000 described previously will incur a net cost of £373,529, and will produce 58.8 extra QALYs. The cost per QALY is therefore £6,349.

- Using probabilistic sensitivity analysis, the paper produces a cost-effectiveness acceptability curve. Using their assumptions, one can be 94.5% certain of sibutramine being cost effective relative to the best non-pharmacological intervention at a threshold of £10,000 per QALY. If this threshold were to increase to £20,000, the likelihood of cost effectiveness described above increases to 99.9%. Although the Institute has no formal threshold, a treatment costing £10,000–20,000 per QALY would usually be considered cost effective.

- Undertaking sensitivity analysis on each of the model inputs, the results are most sensitive to utility gain per kg lost (using the lower 95%CI, the cost per QALY increases to £12,227).

- The use of the old discount rates in the paper does not greatly affect the cost per QALY (the figure rises from £6,349 to £6,840).

Focusing on the reliability of the utility gain per kilogram lost, the 'Health survey for England' presents a slightly different picture. Ara and Brennan assume a uniform improvement in quality of life (QoL) of 0.00375/kg lost.[19] Macran presents more detailed information on this issue, stratifying for BMI levels, age and gender [30]. The QoL figures are presented below. The paper does report QoL figures for BMI of greater than 39 kg/m^2. These are reported in Table 16.16 when the number of observations is 5 or greater.

Table 16.16 Quality of life based on gender, age and body mass index (BMI)

	BMI (kg/m^2)				
	Under 21	**21–25**	**26–30**	**31–39**	**Above 39**
Men (by age group)					
18–24	0.91	0.92	0.92	0.86	
25–34	0.9	0.91	0.92	0.89	0.97
35–44	0.82	0.91	0.89	0.89	0.9
45–54	0.87	0.87	0.86	0.84	0.8

	BMI (kg/m^2)				
	Under 21	**21–25**	**26–30**	**31–39**	**Above 39**
55–64	0.75	0.82	0.81	0.72	
65–74	0.71	0.81	0.81	0.78	
75+	0.8	0.76	0.77	0.76	
All men	0.86	0.87	0.86	0.82	0.88
n	220	2078	2358	779	26
Women (by age group)					
18–24	0.9	0.9	0.9	0.88	0.93
25–34	0.88	0.92	0.91	0.88	0.9
35–44	0.89	0.89	0.86	0.82	0.81
45–54	0.89	0.86	0.83	0.83	0.76
55–64	0.76	0.83	0.78	0.74	0.54
65–74	0.79	0.82	0.76	0.71	0.68
75+	0.64	0.76	0.73	0.68	0.53
All women	0.85	0.87	0.82	0.78	0.75
n	486	2730	1995	1040	115
All	0.85	0.87	0.84	0.80	0.77
n	706	4808	4353	1819	141

Ara and Brennan report utility gain per kilogram lost rather than per BMI point reduction. Therefore, if average male and female heights are assumed to be 180 cm and 165 cm, respectively, the conversion required is shown in Table 16.17. It should be noted that all individual BMI values are rounded to the nearest point to ensure the ranges given below are exhaustive.

Table 16.17 Approximate relation between weight and body mass index (BMI [kg/m^2])

	BMI range	Weight range (kg)		BMI range	Weight range (kg)
Women	< 21	< 57.2	Men	< 21	< 68.0
	21–25	57.2–68.1		21–25	68–81
	26–30	68.1–81.7		26–30	81–97.2
	31–39	81.7–106.2		31–39	97.2–126.4
	39+	106.2+		39+	126.4+

Taking the mid-point of each range,* the weight loss and utility gain can be synthesised into a utility gain per kilogram lost and contrasted with Ara and Brennan (Table 16.18).

Table 16.18 Calculating utility gain per kilogram lost in men and women

	BMI (kg/m^2)	kg lost	Utility gain	Utility gain per kg
Women	28–23	13.6	0.05	0.003676471
	35–28	19.1	0.04	0.002094241
	44–35	24.5	0.03	0.00122449
Men	28–23	16.2	0.01	0.000617284
	35–28	22.7	0.04	0.001762115
	44–35	29.2	–0.06	–0.002054795

The Ara and Brennan assumption of a utility gain per kilogram lost of 0.00375 is reasonable for women at lower initial BMI levels. However, the assumption becomes increasingly unrealistic at higher BMIs and among men. In the sensitivity analysis of Ara and Brennan, the lower boundary of this parameter is set at 0.001/kg lost and leads to a cost per QALY of £12,227. This is probably conservative for women as the estimate for QoL gain per kilogram lost ranges from 0.00122 to 0.00368. A cost per QALY between £6349 and £12,227 is realistic. Among men, the cost per QALY figure is likely to be higher. At the extreme (such as the more obese males), it could be said that the QoL figures presented above show no QoL gain through weight loss per se. Under Ara and Brennan's figures, the removal of this component of benefit increases the cost per QALY to £18,400.

One further parameter which the result will be sensitive to, but is not mentioned in the report, is the rate of weight regain. In the company model, the rate of weight regain, and their source for the figures, are as shown in Table 16.19.

* Clearly, there is no mid-point for the lowest and highest BMI groups. This is not important for the lowest group since moving between BMI levels below 21 is beyond the remit. However, a mid-point of 44 was assumed for the group with a BMI greater than 39 kg/m^2.

Table 16.19 The assumed weight gain in Ara and Brennan[19]

Group	Weight regain (kg/month)	Standard error	Distribution
Responders	0.38486	0.0131	Normal
Placebo	0.36964	0.0131	Normal
Natural history	0.08333	0.0108	Normal

The implication of these figures is that the average responder at all hurdles to sibutramine treatment (thus receiving a 1-year regimen of 10 mg) will return to their original weight in 45 months and their trend weight in 58 months. The clinical review found no conclusive evidence regarding the suitability of this assumption. If this assumption exaggerates the length of time at below trend weight, the cost per QALY will be higher than the estimate given in the paper.

One final caveat is that the clinical advice suggested that the sibutramine treatment given by the paper was an exaggeration of the treatment actually provided. If this is an exaggeration, the true cost per QALY would fall as then treatment is relatively less expensive. Their assumption of healthcare professional contact is as shown in Table 16.20.

Table 16.20 Healthcare contact in the sibutramine group in Ara and Brennan[19]

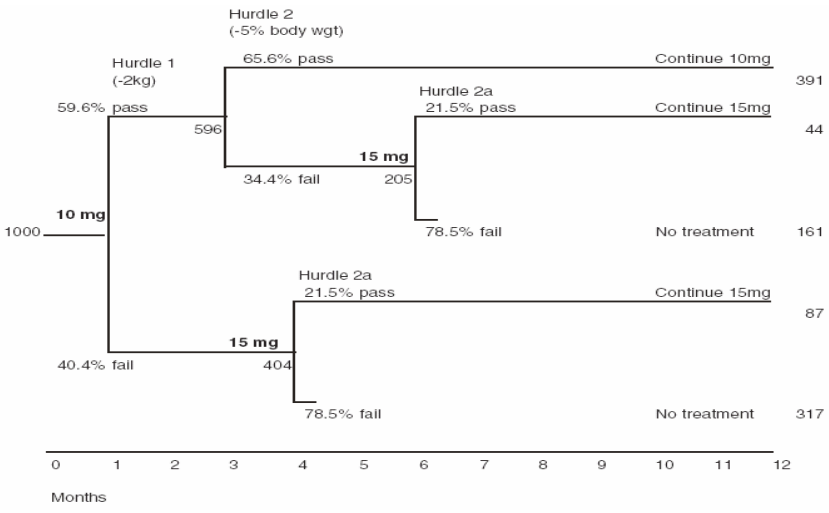
Month	Monitoring
0	All patients have an initial appointment with GP prior to commencing treatment/diet and exercise
1,2,3	Two appointments per month for sibutramine recipients
4,5,6	One appointment per month
9,12	One appointment at month 9 and month 12

An industry-funded paper looked at the cost effectiveness of a 10 mg regimen of sibutramine relative to a group receiving only diet and exercise advice.[31] The population modelled was a cohort of 1000 chosen according to UK prescription data (specifically 20% men, aged 18–65 (mean 42 years) and BMI between 27 kg/m^2 and

40 kg/m^2 [mean 32.7]). After 1 year of treatment, participants were modelled for 5 further years, calculating QoL based upon weight per se, diabetes status and CHD status. The incremental cost per QALY was calculated to be £4780 based on 2003 prices.

The authors undertook a univariate sensitivity analysis on 24 separate model inputs. By altering each of these 24 parameters within pre-defined limits, the cost per QALY remained between £2950 and £9034. The one exception to this was that the model was sensitive to the utility attached to weight loss per se. When this utility gain was set at the lower extreme, the cost per QALY rose to £14,072.

16.4.4 Further analysis



One aspect of the literature the group wanted to investigate was whether hurdle 2a in the product monograph (see above) was a cost-effective intervention, independent of the rest of the treatment. Specifically, given the relatively low success rate at hurdle 2a among people in whom the earlier hurdles failed, does the effect of the 15 mg regimen in this subpopulation represent value for money?

Using the figures from Ara and Brennan[19], 21.4% of people pass hurdle 2a. In their cohort of 1000, this means 131 responders and 478 non-responders (the other 391 do not reach this hurdle). This means each receives the 15 mg dosage for a further 3 months, costing £88,354. Furthermore, the 131 responders will incur drugs costs of £46,426 following success at hurdle 2a (since success means their treatment is

continued for the remainder of the year instead of discontinued). Thus, total drug cost implication of including hurdle 2a is £134,780. Following the approach of Ara and Brennan, this cost is reduced by the decreased incidence of diabetes and CHD by £12,520. In the model, the non-drug costs are comparable between the two groups. Thus this figure represents the incremental cost of including hurdle 2a in the cohort. The net cost per responder of hurdle 2a is £122,260/131 = £933.

> (QALYs (sibutramine group) – QALYs (control group))/Proportion of responders in the total cohort

The denominator shows that this calculation assumes that the gains of sibutramine are isolated to those who respond to the hurdles. Thus, the expected QALY gain in those who respond at hurdle 2a compared with those who do not is:

> (35.508 – 35.449) / (522/1000) = 0.113 QALYs

If this assumption is made, this gives a cost per QALY of £933/0.113 = £8257.

It is important to note that the real cost per QALY is likely to increase from this estimate. This is because this calculation assumes that those who respond to treatment at hurdle 2a have the same profile as those who respond at hurdle 1. It is likely that those who struggle to respond at the first stage but go on to succeed at the latter may have lower total utility gains. To an extent, this may be counteracted because the effect of the more intense treatment among those in whom the treatment still fails, as defined by losing the required weight to continue, will still have some benefit of reduced weight.

16.4.5 Cost effectiveness of sibutramine in obese children and adolescents

There were no cost-effectiveness studies focusing either exclusively or in part on children. However, statements useful in the consideration of cost effectiveness can be drawn from the clinical literature.[32,33] In Berkowitz and co-workers' study, the focus was on 82 adolescents aged between 13 and 17 years, with a BMI between 32 kg/m^2 and 44 kg/m^2. The intervention group received behavioural treatment and sibutramine for 6 months and the control group received behavioural treatment and placebo. From months 7–12, all received sibutramine alone. At 6 months, the

intervention group had reduced BMI by 8.5% (SD 6.8%). Although the use of BMI z-score would have been informative since it allows for the natural development of children over time, this BMI reduction figure compares favourably with that used in the previously discussed Abbott company submission for adults.[34] However, a comparison is difficult since the papers use different treatment protocols. It cannot be determined whether the cost of treatment for obese children would be different from that for obese adults, given the use of the product monograph employed in the company submission.

In the adult literature, the main driver of cost -effectiveness is the reduction of incidence of obesity-related conditions. Although an increased risk of diabetes should be considered as a consequence of obesity in children, it is less sustainable to include myocardial infarction (MI), stroke or cardiovascular disease (CVD) as a direct benefit of the weight loss elicited by the pharmacological regimen. Although these diseases are being seen in extreme cases in younger groups, using them as the only output measures from drug therapy would surely underestimate the benefit children receive from pharmacological interventions.

It is certainly arguable that the benefits of reduced weight in obese adolescents are much less tangible and include issues such as self-esteem and the motivation to alter behaviour. If this is true, the role of health economics is marginal as the measurement of such benefits is much harder than that of reduced incidence of disease.

16.5 Cost effectiveness of orlistat

16.5.1 Cost effectiveness evidence statements (Table 16.21)

Table 16.21 Evidence statements on cost effectiveness of orlistat

1	Orlistat is a cost-effective intervention in adults with a BMI greater than 30 (or 28 with comorbidities) relative to non-pharmacological interventions
2	The most reliable published estimate of a cost per QALY under current licensing is £24,431(range:£10,856-£77,197)
3	Under the alternative European Agency for the Evaluation of Medicinal Products (EMEA) licence as described by Foxcroft,[24] the cost per QALY is £19,005 (range:£8,840-£57,798)
4	There is no published evidence regarding the cost effectiveness of a longer regimen (> 12 months) of orlistat relative to a regimen of 12 months. However, the cost per QALY is likely to increase as the treatment length extends beyond 12 months
5	The incremental cost-effective ratio of a 48-month regimen of orlistat relative to a 12-month regimen ranges from £22,099 to £39,308 per QALY, dependent on gender, initial BMI, the natural rate of weight gain and the rate of weight regain after conclusion of treatment
6	There is no cost-effectiveness evidence regarding the use of orlistat in children and adolescents

BMI, body mass index; QALY, quality-adjusted life year.

16.5.2 Current report – summary and analysis

Consideration of: **O'Meara S, Riemsma R, Shirran L et al. A systematic review of the clinical effectiveness and cost-effectiveness of orlistat in the management of obesity. *Health Technology Assessment* 2001;5:1–81.**

This report was commissioned to provide evidence to the NICE Appraisals Committee. The existing HTA report literature search identified one suitable cost-effectiveness study published prior to their cut-off in June 2000. (Roche. Cost-utility of orlistat. Company submission. 2000) Furthermore, they appraised one company submission. In the literature search result 'Orlistat for the treatment of obesity'[35] the authors used published evidence to provide costs and clinical effects of a regimen of 120 mg three times daily combined with diet relative to diet alone. The clinical data

came from double-blind RCTs.[31;34;36] These data are combined with cost data to produce a cost–utility analysis.

In a hypothetical cohort of 100 patients, the treatment as per the product monograph costs £73,436. Under the base case, the number of QALYs gained in a year are 1.601. This equates to £45,881 per QALY gained. The authors produced a sensitivity analysis, illustrating the responsiveness of this cost per QALY to changes in the base case assumptions. Altering annual costs, dropout rates, response rates and utility gain gradients within reasonable parameters, the cost per QALY remained between £13,541 and £131,918. In their analysis, Foxcroft and Ludders did not include side effects such as gastrointestinal problems and vitamin malabsorption because it was felt these were *'*mild and transient*'*.

The other cost-effectiveness paper covered in the HTA report was a company submission by Roche. The company have updated this model.[24]The details of their new analysis are provided later in this narrative.

16.5.3 Literature search

The cost-effectiveness literature search for the use of orlistat for obesity focused on the period following the cut-off in the original report (June 2000). This identified two studies, both of which were of a suitable standard. Both were cost-effectiveness or cost-utility models, based in developed countries and had orlistat treatment as part of the treatment branch. Further to this, there was one company submission. All of these studies focused specifically on adults.

Since no cost-effectiveness studies on the use of orlistat in children and adolescents were identified, the clinical search results were used to provide guidance on the formulation of recommendations in this group.

16.5.3.1 Cost-effectiveness results for papers published after June 2000

A company submission looks at the cost effectiveness of orlistat treatment based on previous NICE guidance for England and Wales.[24] The clinical information comes from three European trials. [24,37,38] The paper also looks at the European Agency for the Evaluation of Medicinal Products (EMEA) approach (treatment discontinued if weight loss < 5% at 3 months).

In line with the SPC at the time, NICE guidance (TA22) gave conditions for the initiation and continuation of treatment. These included a 'starting criterion':

1. Orlistat should only be prescribed for people who have lost at least 2.5kg by diet and exercise alone in the preceding month.

As well as two 'stopping criteria':

2. Continuation beyond three months should be supported by evidence of a loss of at least 5% of body weight from the start of treatment.

3. Continuation beyond six months should be supported by evidence of a cumulative loss of at least 10% of body weight from the start of treatment.

Foxcroft estimated that the use of the NICE-specified population reduced the cost per QALY to £24,431 (£19,005 under the EMEA approach).

The paper used a utility gain per kilogram lost of 0.017. Using 'Health survey for England' figures given in the sibutramine section above, this is a realistic assumption for the general population. The rate of utility gain seems to differ between subgroups, being relatively low in the most obese, and in men. The major change in the costs attributed to treatment was that, unlike the previous company submission, prescriptions were performed in primary care rather than in specialised hospital units (thus reducing the cost).

In this analysis, five GP contacts were required. These were the initial consultation, one at the start of treatment, one at 3 months and two between 3 and 12 months (if there is a hurdle at 6 months, one of these must fall at this point).

The sensitivity analysis in the paper showed the cost per QALY results had lower and upper boundaries of £10,885 and £77,196 for NICE criteria and £8839 and £57,798 for the EMEA criteria. The upper boundaries occurred in a situation with some healthcare professional contacts occurring in a secondary care setting and utility gain from weight loss per se reduced to an arbitrary value of 0.05 QALYs gained per effective year of treatment.

As noted above, the paper included a comparison of the cost-effectiveness of orlistat use under NICE criteria (1, 2 and 3 above) and under 'EMEA' criteria (1 and 2 only). The results suggest that treatment under EMEA criteria is cost-effective: £19,000 per QALY (range £8,800 to £57,800 in sensitivity analysis).

Scenario	Criteria	Cost	QALYs	ICER*
Base case	NICE (1,2 & 3)	£22,745	0.931	£24,431
	EMEA (1 & 2)	£27,824	1.464	£19,005
high QALY/ low cost	NICE (1,2 & 3)	£14,742	1.358	£10,856
	EMEA (1 & 2)	£19,359	2.19	£8,840
high QALY/ high cost	NICE (1,2 & 3)	£28,949	1.358	£21,317
	EMEA (1 & 2)	£34,968	2.19	£15,967
low QALY/ low cost	NICE (1,2 & 3)	£14,742	0.375	£39,312
	EMEA (1 & 2)	£19,359	0.605	£31,998
low QALY/ high cost	NICE (1,2 & 3)	£28,948	0.375	£77,195
	EMEA (1 & 2)	£34,968	0.605	£57,798

* Incremental Cost-Effectiveness Ratio: each option compared with non-pharmacological treatment. Note that for all scenarios NICE criteria are subject to extended dominance.

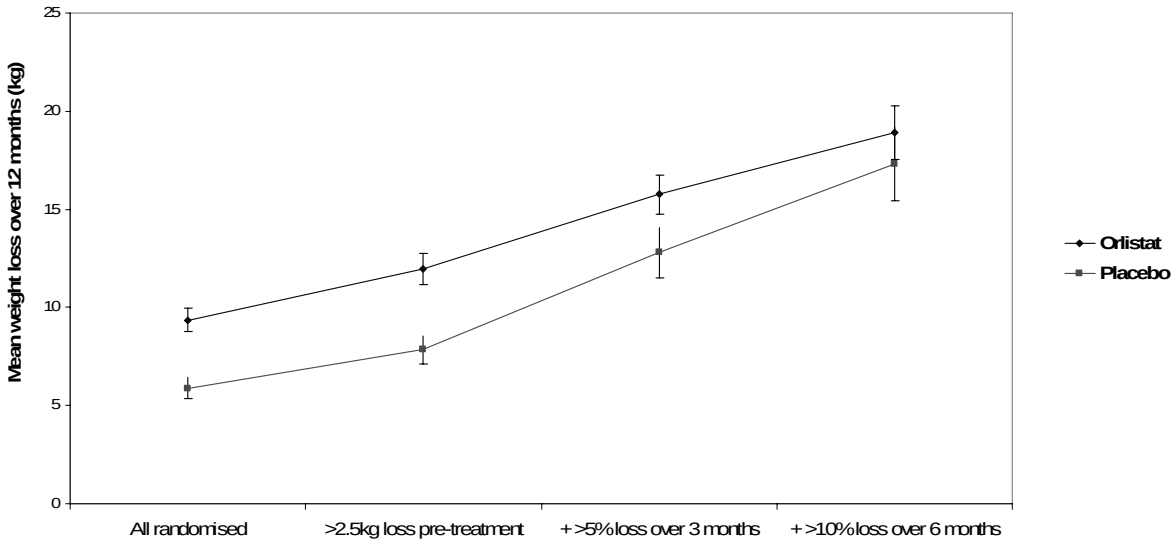
Although the 6-month stopping criterion reduces costs, it does not appear to be a cost-effective addition: the estimated cost per QALY under NICE criteria (£24,400, range £10,900 to £77,200) is higher than under EMEA criteria. However, this rather counterintuitive result could be a consequence of the method used to estimate QALY gains by Foxcroft.

For the EMEA criteria, it was assumed that patients who met 3-month criterion achieved a QALY gain proportional to their mean weight loss over twelve months: with orlistat (compared with placebo) an additional 12.1% of patients met the 3 month criteria and these patients lost an additional 2.95 kg over 12 months. This mean weight loss was then converted to a mean loss in BMI (assuming a mean height of 1.66m), and then to an expected QALY gain (assuming a gain of 0.017 QALYs per unit loss of BMI). It was assumed that patients who stopped treatment at 3 months received no benefit.

For the NICE criteria, it was assumed that only patients who passed the 6-month hurdle would gain any benefit: with orlistat an additional 7.5% of patients passed this hurdle, gaining a mean additional weight loss of 1.6kg each. However, patients treated for between 3 and 6 months under the NICE criteria are also likely to have

achieved additional weight loss and hence QALY gain. Furthermore, it is not apparent why the mean 12-month weight loss should be lower for patients who pass the 6-month hurdle than for those who pass the 3-month hurdle. This could reflect sampling error due to the relatively small number of placebo group patients passing the 6-month hurdle (37 out of 696 patients randomised to placebo, compared with 90 out of 702 randomised to orlistat). It can be seen that the difference in mean weight loss over 12 months is not significant for the subgroup of patients who pass the 6-month stopping criteria (see graph below).

Figure 1. Twelve-month weight loss for all patients and for subgroups responding to pre-treatment, 3-month and 6-month criteria (data from Foxcroft 2005)



The other assumptions in the model appear to be reasonable, and are not expected to introduce bias in favour of orlistat treatment – if anything the model is relatively conservative. However, Foxcroft does discuss some other limitations to the study. Notably, that data beyond one year follow-up, which could show rebound weight gain, was not made available for the analysis. Further, data on a large North American trial was not provided. Foxcroft comments that the results from the two European trials included in the modelling were 'broadly compatible' with those from a Cochrane review: mean one-year weight loss, compared with placebo, of 3.45kg and 2.7kg, respectively. The impact of this discrepancy on the estimated cost-

effectiveness cannot be tested as the results are not available separately for 'responders' and 'non-responders' at 3 and 6 months.

Conclusion: There is no estimate of the impact on cost-effectiveness of removing the requirement that patients lose at least 2.5kg in the month preceding prescribing of orlistat. Cost-effectiveness evidence presented in both the appraisal and the guideline includes this assumption.

There is some evidence to support removal of the requirement that at least 10% of body weight is lost by 6 months for continuation of treatment. One industry-funded model estimated that treatment would be more costly, but also more cost-effective if this requirement were to be removed. However, there are reasons to question the robustness of this conclusion because of some of the modelling assumptions and the exclusion of some relevant data.

One other paper was identified: a Roche-funded Belgian study looked at the cost effectiveness of a 2-year orlistat regimen in an obese (BMI > 30 kg/m^2) Belgian population compared with no treatment.[39] The population was stratified according the occurrence or not of hypercholesterolaemia and hypertension (meaning four subgroups). The authors synthesised the costs and life years gained (LYG) attributable to the intervention. They concluded that the cost per LYG ranged from €3,462 for obese diabetic people with hypertension and hypercholesterolaemia to €19,986 per LYG for obese diabetic people without risk factors.

A response to this article[40] highlighted further problems with the conclusions of this paper, specifically their choice and application of model parameters. The two major issues raised concerning their choice of model parameters were that:

- The author looks at the impact of reductions in HbA1c levels on the risk of macrovascular complications. They used the Diabetes Control and Complications Trial which includes only type 1 diabetic patients. Lamotte and coworkers[39] use these figures on macrovascular complications for people with type 2 diabetes. It is usual to consider that the relation between macrovascular complications and HbA1c is unlikely to be comparable between the variants of diabetes.

- Lamotte and coworkers[39] use the Helsinki Heart Study (HHS) to estimate the relation between low-density lipoprotein (LDL)-cholesterol and coronary events in people with type 2 diabetes. Edelsberg et al.'s response[40] claims that this study has been discredited as underpowered and concludes that figures used understate cost-effectiveness ratios.

The final result from the literature search was an American study[27] comparing the use of orlistat (120 mg, 3 times daily) for 52 weeks plus standard diabetes therapy (sulphonylurea, metformin or insulin) and weight management with standard diabetes therapy and weight management in obese and overweight diabetic people. The authors built a Markov model, populating it with transition probabilities and utility states. These data on the effectiveness (and side effects) of orlistat[34;41;42] complication rates[43] and costs[44–45] came from a variety of published sources. They concluded there was an incremental cost of US$1,122 (2001 values) and an incremental life year figure of 0.13. Combining the two, there is a cost per life year gained of $8,327. At face value, this figure seems to suggest cost effectiveness of the intervention relative to the control. However, this study had some drawbacks.

First, the disease incidence rates were representative of a small demographic (age 50–54, male, Caucasian, diabetic people, duration of diabetes 7.5–12.5 years). Significantly, the authors noted that complications among women occurred at half the rate of men. If the complication rate falls, it is likely that the cost effectiveness reported as baseline was an underestimate. Second, the conclusion was sensitive to the duration of weight loss. In the base case, they assumed responders took 3 years to return to weight trend. However, if this figure was 1 year, the cost per life year gained would rise to around $20,000. The final caveat is that, although effect size is taken from a UK population (so is relevant for this analysis), costs may not be transferable from the USA.

16.5.4 Cost effectiveness of other lengths of treatment relative to a 12-month approach

Most studies follow existing guidance on length of treatment. Therefore, the literature on extending treatment is limited. There are no cost-effectiveness papers that look at this issue. One clinical study that looked at the role of orlistat in lowering weight and

the incidence of diabetes over 4 years.[46] The results presented in the clinical review show that the effect of orlistat beyond 1 year of treatment is to slow down the rate of weight regain. The orlistat group regained 4.8 kg between 12 and 48 months compared with 3.2 kg in the placebo group. The weight regain rate was therefore 133 g per month in the orlistat group. At 48 months, the intervention group had lost an average of 2.8 kg more than those in the control group. Because of the study design, the counterfactual, specifically the rate of weight regain the orlistat group would have experienced between months 12 and 48 had it not been on orlistat, was not given. To investigate this issue, independent modelling (described below) was undertaken within the collaborating centre.

The average pathway of BMI over time under the 12-month and 48-month regimen can be simply modelled using Torgerson and coworkers'[46] results and the evidence from Davidson and coworkers[31] and Sjostrom and coworkers[36] on weight regain. Assuming a linear pathway of BMI (other than the switch at 12 months from weight loss to weight regain), this pathway can be illustrated diagrammatically (Figure 16.1).

Figure 16.1 Pathway of weight over time under different orlistat programmes (initial body mass index [BMI] of 33 kg/m^2)

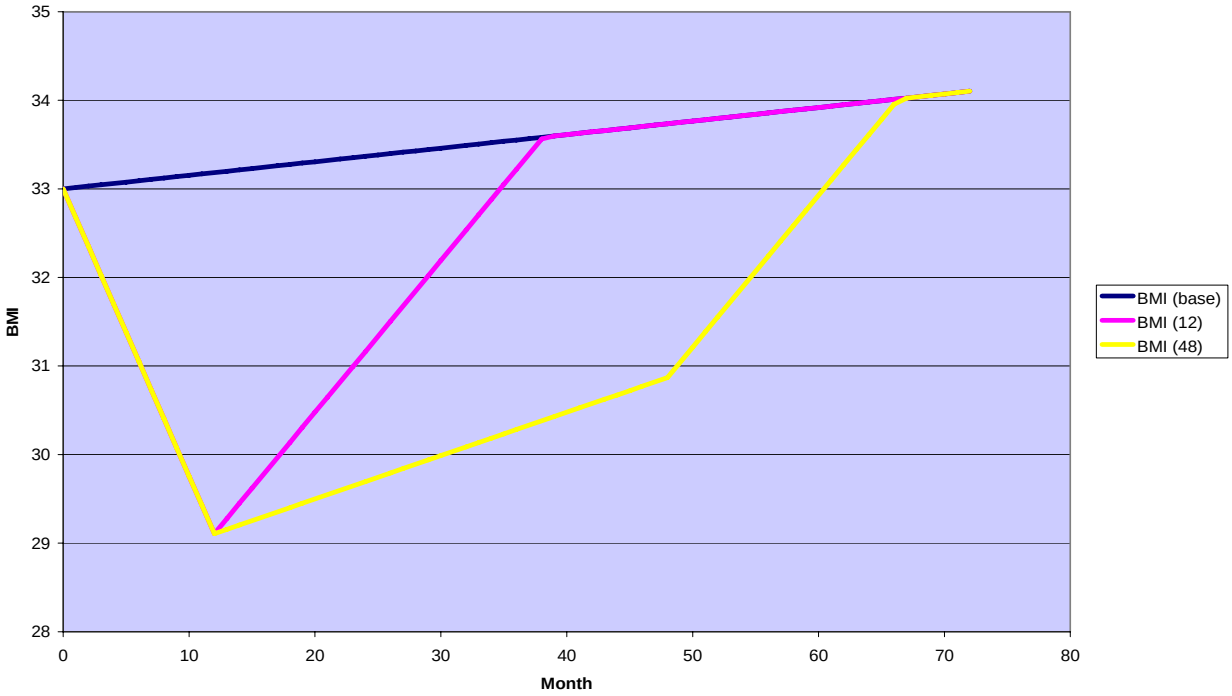


Figure 16.1 shows the path for trend weight regain and BMI over 12- and 48-month regimens in a person with an initial BMI of 33 kg/m^2. The model assumes that the rate of weight regain is the same at the end of the treatment period, be it 12 or 48 months.

The model investigates the costs and benefits of this weight reduction in terms of QoL improvements through weight loss per se, CHD, type 2 diabetes and colorectal cancer, as well as the relation between BMI and mortality. Each BMI level will be associated with a prevalence of the three conditions, a QoL figure independent of disease, and a mortality rate.

Various company submissions have suggested a QoL/weight (or BMI) gradient.[19] However, these estimates assume a constant gradient, an assumption which is unlikely to be realistic. Therefore, estimates were taken from a paper which did identify a different gradient at different BMI levels. [30] This paper provided QoL estimates for five BMI ranges (< 21, 21–25, 26–30, 31–39 and > 39). These figures were ascribed to the central values of each range and a linear trend between mid-points was assumed. Thus, expected QoL values were estimated for each 0.1 increment of BMI.

Information on diabetes prevalence by BMI level was also attained.[47] The principle used was to estimate the likelihood of diabetes at each BMI level, amend the cost of orlistat to reflect the cost offset through reduced diabetes prevalence, and to weight the expected QoL estimates accounting for the disutility this chronic condition brings. A utility multiplier of 0.8661 was identified in the literature and assumed.[19]

The costs of diabetes were developed using the approach of Ara and Brennan.[19] However, it was felt that type 2 diabetes was more likely to be managed in primary care. Therefore, treatment was assumed to contain visits and treatment as shown in Table 16.22.

Table 16.22 Diabetes care suggested by Ara and Brennan[19]

Visit/test/treatment	Units per year	Unit cost (£)	Total cost per year (£)
GP nurse	2	8	16
Specialist nursing	1	22	22
GP clinic	2	15	30
HbA1c test	1	6.5	6.5
Home glucose test	12	0.27	3.24
Eye screening	0.5	10.5	5.25
Angiotensin-converting enzyme inhibitor – ramipril			117
Diuretic			9
Statin therapy (simvastatin)			387
Metformin antiglycaemic therapy			37

CHD figures were identified, stratifying risk of CHD by BMI level.[48] These risk ratios were smoothed by attributing the value of each BMI range to the central value and joining these. The cost of CHD was taken from global costing figures.[49] The paper suggests that 988,000 people received treatment at a total cost of £716 million. This gives an approximate average value per person per year of £725.

The prevalence of colorectal cancer by BMI was calculated by combining data on the relative risk of the condition by BMI level[50] with the prevalence of colorectal cancer in the general population.[51] No UK studies identified a cost of treating colorectal cancer. However, an Australian paper[52] identified a cost of Aus$18,435, which was converted to UK currency and applied as the best cost estimate.

The costs of orlistat treatment are calculated to be the cost of 120 mg three times per day for either 12 months or 48 months (Table 16.23). Since Torgerson's[49] data include lifestyle advice, the model assumes four GP visits in each of the subsequent years of continued treatment. The cost of this is derived through research undertaken by the Personal Social Services Research Unit.[10]

Table 16.23 Baseline results for the cost-effectiveness of longer treatment regimens (genders combined)

	12 months vs 0	48 months vs 0	48 vs 12 months
QoL gains	0.0551	0.1104	0.05526
Cost difference	584	2 130	1 545
Cost/QALY	10 600	19 292	27 965

QALY, quality-adjusted life year; QoL, quality of life.

The incremental cost-effectiveness ratio for a 12-month regimen is comparable to that presented elsewhere. The driver for the slightly lower value is that the efficacy data come from Torgerson and coworkers[46] who suggested a relatively large fall in weight over the first 12 months. The appropriate comparison for the 48-month regimen is the 12-month regimen rather than no treatment. Thus, the cost per QALY in both genders is £25,407. The use of these figures should contain two caveats.

First, the model excludes the effect of orlistat on the occurrence of other conditions. Thus, it underestimates the true benefit. Second, the sensitivity analysis suggests the conclusion does alter as various model parameters (gender of the person, initial BMI, trend weight gain and the rate of weight regain once orlistat treatment is discontinued) alter (Table 16.24).

Table 16.24 Sensitivity analysis for longer treatment regimens

Variable	Value	Cost per QALY (£) (12 months vs 0)	Cost per QALY (£) (48 months vs 12)
Baseline	See below	Male 10,643	Male 29,089
		Female 10,556	Female 26,917
In the base case, initial BMI is 33 kg/m^2, trend weight gain is 0.5 kg/year, and weight gain after discontinuation of treatment is 5.6 kg/year			
Initial BMI	30	Male 13,182	Male 33,134
		Female 10,229	Female 23,982
	38	Male 11,237	Male 29,920
		Female 12,505	Female 30,115
Trend weight gain	0	Male 12,604	Male 36,704
		Female12,448	Female 33,884
	1	Male 9,238	Male 23,923
		Female 9,198	Female 22,099
Weight regain post discontinuation	3.6	Male 7,607	Male 39,308
		Female 7,408	Female 35,486
	7.6	Male 12,982	Male 25,985
		Female13,033	Female 24,249
Cost of type 2 diabetes care p/a	£1,550 (as per CODE2)	Male 9,806	Male 27,985
		Female 9,509	Female 25,648

QALY, quality-adjusted life year.

The results suggest that the cost per QALY depends on the gender of the person, the initial BMI, the cost of treating type 2 diabetes, the trend weight gain without orlistat and the rate of weight regain once orlistat treatment is discontinued. However, within these limits, the incremental cost-effectiveness ratio ranges from £22,099 to £39,308. In comparison with other economic analyses in the Institute, this suggests that the intervention cannot be firmly recommended on cost-effectiveness grounds.

16.5.5 Cost effectiveness of orlistat for obese children and adolescents

There were no cost-effectiveness studies focusing either exclusively or in part on children. However, some guidance might be drawn from the clinical literature which can be used in the cost-effectiveness discussion of orlistat use in obese adolescents.

In both located clinical trials amenable to health economic analysis[53,54] the authors treat children according to the adult dosage (120 mg three times daily). However, McDuffie and co-workers' discontinued treatment after 3 months (contrasting with 1 year by Ozkan and co-workers'). If a shortened period of treatment for adolescents was part of any treatment protocol, this would clearly lead to a significant reduction in drug costs. The pertinent question for cost-effectiveness purposes is then whether there is a clinically worthwhile difference between the 3-month treatment (combined with a diet, exercise and behaviour course) and a similar longer treatment (11.7 $\pm$ 3.7 months[53]). Unfortunately, the clinical results do not provide a clear answer since the populations were small (20 in McDuffie,[54] 22 in Ozkan[53]) and may have undertaken radically different lifestyle, diet and behavioural interventions. Both studies suggest a higher dropout rate among children than among adults (32% in Ozkan,[53] 15% in McDuffie[54]). This has cost-effectiveness implications since the expected beneficial effect of treatment is diluted by dropouts.

While the costs may be lower in the orlistat treatment of obese adolescents, the benefits as measured by the adult cost-effectiveness literature may also be lower. However, this may be a consequence of adults and children having different relevant endpoints when prescribed pharmacological interventions for obesity.

In the adult literature, the main driver of cost effectiveness is the reduction of incidence of obesity-related drugs. While an increased risk of diabetes should be considered as a consequence of obesity in children, it is less sustainable to include MI, stroke or CVD as a direct benefit of the weight loss elicited by the pharmacological regimen. Although these diseases are being seen in extreme cases in younger groups, using them as the only output measures from drug therapy would surely underestimate the benefit children receive from pharmacological interventions.

It is certainly arguable that the benefits of reduced weight in obese adolescents are much less tangible and include issues such as self-esteem and the motivation to alter behaviour. If this is true, the role of health economics is marginal as the measurement of such benefits is much harder than that of reduced incidence of disease.

16.6 Cost effectiveness of surgery

16.6.1 Evidence statements related to surgery for obesity (Table 16.25)

Table 16.25 Evidence statements

1	Evidence suggests that surgery in general is a cost-effective intervention relative to a limited non-surgical management option in a typical severely obese group
2	The most reliable cost per QALY estimate is £6289 to £8527

16.6.2 Surgical developments in the period 2001–05

The approach in this report is to consider gastric bypass, gastric banding and the biliopancreatic diversion/duodenal switch (DS-BPD) as the major surgical interventions for consideration. The reason for this, that these best represent the surgical options facing healthcare providers, is described in the clinical review in Section 15.3.5.

16.6.3 Existing report

Consideration of: **Clegg AJ, Colquitt J, Sidhu MK et al. The clinical effectiveness and cost-effectiveness of surgery for people with morbid obesity: a systematic review and economic evaluation. *Health Technology Assessment* 2002;6:1–153.[55]**

Note: Since this review, the vertical banded gastroplasty (VBG) has become obsolete, having been replaced by the laparoscopic gastric bypass. Details on the vertical banded gastroplasty are given where relevant but otherwise have been removed.

The economic component of the HTA report is split into two broad sections. First, the authors undertook a comprehensive literature review and found four economic evaluations of a suitable quality, all produced from outside England and Wales. The results of this are described below. The second step was to produce a model, synthesising cost and benefit data into measures of cost effectiveness for Roux-en-Y gastric bypass, vertical banded gastroplasty, adjustable gastric banding and non-surgical management. This model is described below. The original intention of this

guidance group was to re-run the modelling with updated assumptions based on newer literature. Unfortunately, the group that was responsible for the preparation of this model was unable to release it. Therefore, this discussion describes the assumptions that need updating to reflect current practice and the likely effect these changes would have on the cost per QALY.

16.6.3.1 The HTA literature search results

The HTA identified four relevant papers, two of which investigated the vertical banded gastroplasty (thus being of limited usefulness to this discussion). An American study compared Roux-en-Y gastric banding with a very-low-calorie diet (VLCD) for at least 12 weeks and weekly behavioural modification meetings for at least 4 months.[56] A total of 201 participants entered surgical and 161 entered medical therapy. They were followed for 6 years after the treatment. Surgical therapy was costed at US$24,000, and the control was US$3000. Rather than calculating QALYs, the paper uses pounds lost as the outcome for the economic evaluation. If participants lost to follow-up are included, the cost per pound lost in surgery was between US$250 and US$750. This compares with the figures for the control of between $100 and $1600. The authors noted that longer-term follow-up would improve the relative position of surgery since the weight loss from this approach continues beyond 6 years, in contrast with their observations of other approaches.

A Swedish study looks at the cost effectiveness of gastric banding, vertical banded gastroplasty and gastric bypass relative to conventional management.[57] The authors noted that the definition of conventional management was not adequately defined. Data from this Swedish Obese Subjects (SOS) trial was used to estimate prevalence rates over 10 years for hypertension and diabetes between surgically -treated groups and conventionally treated control subjects. Using officially published Swedish costs of treatment, the total cost attributable to these diseases will be on average SEK2700 (£199 as of August 2005)/subject/year higher in the control group. However, the authors note that the cost implication of these diseases is likely to overlap. Second, there will be other diseases which should be factored in to produce an accurate cost of illness figure.

16.6.3.2 The HTA modelling

Below is an exposition of the HTA method and results. As stated previously, the limitations of the useful health economics data published since the HTA means that the best approach is to assess where the original model uses outdated assumptions and the likely effect of replacing these with those representing current practice.

The authors† illustrate four areas of potential benefit from surgery for severe obesity. These are:

- excess weight reduction and the gains in health-related quality of life (HRQoL) through weight loss per se
- gains in HRQoL as a result of reduced morbidity from diseases resulting from obesity
- benefit of death averted through reduction in weight and weight-related illnesses
- indirect benefits from the above areas, such as gains in economic productivity.

Each of the components of benefit are a function of the initial level of BMI and the loss attributable to the surgery. The quality of life gain through weight loss per se is based on a company submission from Roche[58] on orlistat cited in the orlistat section (section 16.5). The assumption is that utility gain due to a 1 BMI point reduction is 0.0159 in males and 0.0166 in females. In the Sibutramine section (section 16.4) of this report, it is illustrated that this is an unrealistic assumption, especially in males. Tables 16.16–16.18 estimate the utility gain per BMI point reduction in various subpopulations. If the QoL improvements calculated using the 'Health survey for England' figures are more accurate, the cost per QALY will rise from that stated in Clegg's analysis.[55]

The HTA report ran a model using a hypothetical cohort of 100 patients. The members of the cohort had an average weight of 135 kg, average BMI of 45 kg/m^2, average age of 40, and 90% were women. Under each of the treatment options, the

† Clegg AJ, Colquitt J, Sidhu MK et al. The clinical effectiveness and cost-effectiveness of surgery for people with morbid obesity: a systematic review and economic evaluation. *Health Technology Assessment* 2002;6:1–153.

cohort was observed for 20 years after surgery. Costs were discounted at 6% per year and benefits at 6%, 0% and 1.5%.

The authors began by creating efficacy scenarios. This was an attempt to create a consensus from the clinical literature outlining the expected efficacy of the different types of surgery. Details of how they came to their assumptions are provided in the HTA report. The baseline assumptions regarding weight reduction, actual weight and BMI levels are presented in Tables 16.26 and 16.27.

Table 16.26 Percentage weight loss over time under gastric bypass, vertical banded gastroplasty, adjustable silicone gastric banding and non-surgical management

Year	Gastric bypass	Gastric banding	Non-surgical
1	36	20	0
2	36	28	0
3	36	31	0
4	36	30	0
5	36	33	0

Note that these gains used in Table 16.26 are relative to baseline rather than cumulative.

Table 16.27 Body mass index ([BMI] kg/m^2) under the treatment options over time

Year	Gastric bypass	Gastric banding	Non-surgical
Baseline BMI	45	45	45
1	29	36	45
2	29	32	45
3	29	31	45
4	29	32	45
5	29	30	45

The authors presume that the year 5 condition is permanent for people undergoing gastric bypass and gastric banding.

Since VBG is obsolete and the DS-BPD is now being used, the comparable BMI pathway over time needs to be calculated to compare options. These figures can be approximated using a study looking at the DS-BPD.[59] The paper reports excess weight lost at 2, 4, 6 and 8 years. Mean per cent loss initial excess weight (IEW) at 2, 4, 6 and 8 years was 78, 75, 78 and 77, respectively, in the patients with IEW up to 120% and 74, 73, 73 and 72, respectively, in those with IEW more than 120%. Using the population described in the HTA modelling (falling into the less obese group in the Scopinaro paper[60]), this translates to a BMI at 2, 4, 6 and 8 years of 27.45, 28.125, 27.45 and 27.675, respectively. Thus, it is reasonable to assume that the DS-BPD is at least as effective in terms of weight loss as the other surgical options.

The model then included the effect of surgery for the severely obese on diabetes rates alone. Evidence on prevalence of diabetes in severely obese patients was varied. Looking at 11 clinical papers reporting diabetes prevalence, the authors took 10% to be a reasonable baseline assumption. They then assumed that 75% of people are off medication at 3 years. In the baseline, it was assumed that this continued until year 8 (as per SOS) when previous prevalence was reasserted. Incidence rates were taken from SOS, suggesting 2.3% per annum without surgery or 0.45% with surgery. The effect of diabetes reduction on mortality was not included in the baseline analysis since the clinical evidence was considered unreliable. Regarding the cost of diabetes, the authors used the CODE2 study of people with type 2 diabetes. This suggested a cost of £1550, including all diabetes-associated costs and complications.

16.6.3.3 Costs of surgery and complication rates

Gastric bypass

First, the HTA report considered preoperative costs. Under baseline, it assumed for each surgical patient, two underwent work-up and four were screened for suitability. Furthermore, each patient received seven outpatient visits, four dietitian consultations and one session with a psychologist. Regarding surgery, there was further complication in that approximately 10% of gastric bypass was undertaken as an open procedure. Thus, the authors costed 235 minutes in surgery, 6 days postoperative stay and intensive care unit (ITU) admittance for 7.6% of patients for

the patients undergoing a laparoscopic gastric bypass. For the open procedure patients, the figures were 147.5 minutes, 7 days and 21.1% of patients.

Additional complications and procedures were assumed to be:

- mortality – 1%
- incisional hernia – 5% after open operation (based on 10% hernia rate, with half the patients having their repair alongside apronectomy)
- apronectomy in 10% after 3 years.

The HTA report assumed that standard postoperative healthcare contacts were delivered as shown in Table 16.28.

Table 16.28 Postoperative healthcare contacts in gastric bypass patients

	GP	Practice nurse	District nurse	Outpatient clinic contacts	Community dietitian contacts	Psychology consultation
Month 1	6	2	4			
Year 1				4	12	2
Year 2				4	4	2
Year 3+				2	2	1

Adjustable silicone gastric band (ASGB)

Preoperative and postoperative costs were as per gastric bypass. In the baseline analysis, surgical costs for the laparoscopic approach were based on:

- 150 minutes in theatre
- 5 days preoperative inpatient ward stay
- 1 night in either ITU or high-dependency unit (HDU)

Under the assumption that 8% of patients needed an open operation, they required on average:

- 76 minutes in theatre

- 6 days on ward
- 1 night in either ITU or HDU.

The complication rates were as per VBG except that:

- reservoir infection – 5% (all requiring revision surgery)
- band leakage – 5% (requiring revision surgery)
- band slippage – 5% (all requiring revision surgery).

Patients undergoing laparoscopic banding needed 2.9 days in hospital post discharge and patients undergoing open banding required 4.6 days. This includes dealing with hernia repair and cholecystectomy.

Non-surgical management

Annual follow-up involved:

- four GP visits
- two dietitian contacts
- two practice nurse contacts
- two district nurse contacts
- every 3 years – VLCD for 12 weeks (two cans of Slim-Fast daily).

The authors then used published costs to calculate the expected costs of the treatment regimens outlined above.

16.6.3.4 Current practice

It is important to note that expert advice has highlighted that assumptions on resource use given above may no longer represent current practice.

It was suggested that in general, the support contacts reported in the HTA, both preoperative and postoperative, exaggerated current practice. If modelling was

undertaken in this area, this clinical expertise should be combined with the clinical evidence review to produce more realistic assumptions.

Regarding gastric banding, it was suggested that:

- with regard to preoperative care, a patient could expect one outpatient contact and one dietitian contact
- an average of 90 minutes in theatre was realistic rather than the 120 minutes assumed in the HTA
- patients would only be admitted 1–2 days prior to surgery at the earliest
- mortality was likely to be below the assumed 0.5%
- reservoir infection was likely to be below the assumed 5%
- band leakage was possibly below the assumed 3%
- with regard to postoperative care, a patient can expect fewer than six GP contacts, two practice nurse visits and four district nurse visits in the first month
- a patient can expect less than 12 community dietitian contacts and two psychology consultations in the first year after the surgery
- a patient can expect fewer than four dietitian visits and two psychology consultations in the second year after the surgery
- a patient can expect fewer than two dietitian visits and one psychology consultation in subsequent years.

Regarding gastric bypass, it was suggested that:

- with regard to preoperative care, a patient could expect one outpatient contact and one dietitian contact
- conversion rate from laparoscopic bypass to open occurs in around 2%, rather than the assumed 10%

- with regard to postoperative care, a patient can expect fewer than six GP contacts, one to two practice nurse visits and four district nurse visits in the first month
- a patient can expect less than 12 dietitian contacts and two psychology consultations in the first year after the surgery
- a patient can expect fewer than four dietitian visits and two psychology consultations in the second year after the surgery
- a patient can expect fewer than two dietitian visits and one psychology consultation in subsequent years.

Furthermore, the group's co-opted expert suggested that complication rates are likely to be below that of the HTA model. This is due in part to increased experience of bariatric surgery in England and Wales, and partly a result of an increased proportion of operations being performed laparoscopically. The advantage of laparoscopic surgery is twofold. First, it has the capacity for reducing healthcare resource use. Second, there is mixed evidence which suggests it has the possibility of reducing complication rates.[60–61] The acceptance and inclusion of both of these trends into the HTA modelling is likely to reduce the incremental cost-effectiveness ratio. Regarding the cost of surgery, Table 16.29 shows the total cost of the surgical options assumed in the HTA report.

Table 16.29 The cost of surgical options in the HTA report[55]

Surgery option	Laparoscopic	Open
Vertical gastric banding	*£3223*	
Gastric bypass	£3992	£3 333
Adjustable silicone gastric band	£4450	£4 753
Non-surgical care	£336	

Since the original model was not released, it is not clear how resource use was integrated into the model. Therefore, it is difficult to estimate the effect of the changes outlined above on the results presented below. However, it seems the original model overestimated the support costs of surgery. Based on this, it is likely

that, ceteris paribus, the cost per QALY stated in the HTA model will fall with the updated assumptions.[‡] No good-quality alternative costing data were identified in the development of the guidance. However, national Reference Cost figures for surgery on the stomach suggests a baseline cost of £5190 for complex procedures.

16.6.3.5 HTA modelling results

Using the previously discussed cohort of 100 patients, the combinations of costs and benefits under each treatment option was compiled as in Table 16.30 (modified from Table 27 in the original report).

Table 16.30 Benefits and costs of the three surgical options and usual care (table adapted from the HTA report)[55]

Intervention	QALYs	Total net cost (£)
Usual care	1,123	696,415
Vertical gastric banding	*1.149*	*962,690*
Adjustable silicone gastric band	1.168	1,079,516
Gastric bypass	1.167	976,435

QALY, quality-adjusted life year.

Using these figures, we can create a cost-effectiveness ratio for each surgical option relative to usual care (Table 16.31 and Figure 16.2).

Table 16.31 Cost-effectiveness of each surgical options

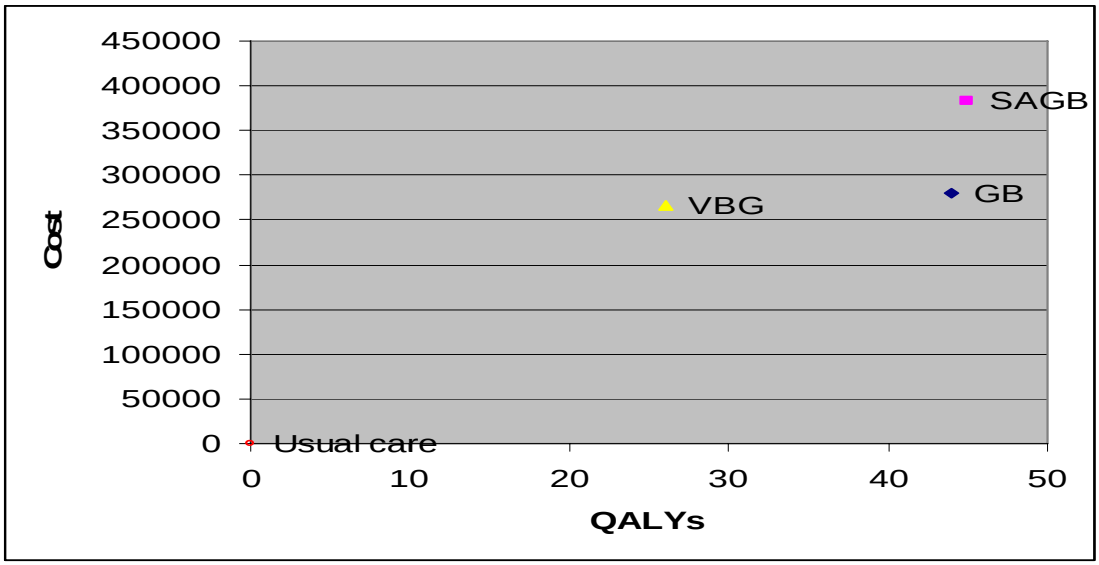
Surgical option	Cost per QALY (£)
Vertical gastric banding	*10,237*
Adjustable silicone gastric band	8,527
Gastric bypass	6,289

QALY, quality-adjusted life year.

Figure 16.2 The incremental costs and benefits of the three surgical options relative to usual care (Note: the incremental cost-effectiveness ratios for gastric

[‡] It should be noted that a Dutch economic evaluation was published subsequent to the guidance literature cut-off and corroborates this improvement on cost effectiveness (van Mastrigt GAPG, van Dielen FMH, Severens JL, et al. One-year cost-effectiveness of surgical treatment of morbid obesity: vertical banded gastroplasty versus Lap-Band. *Obesisty Surgery* 2006;16:75–84). This reports Lap-Bands as dominating the control, suggesting it actually reduces total costs for the health service.

bypass (GB) against vertical gastric banding (VBG) and for adjustable silicone gastric band (ASGB) against GB are £742 and £256,856, respectively)[§]



The conclusion the authors drew was that each of the options is cost-effective relative to usual care. They warn that comparison between surgical interventions is difficult and unlikely to produce a definitive answer. However, they do argue that the results, if taken at face value suggest gastric banding to be the most cost-effective option.

The authors undertake a sensitivity analysis based on areas considered most uncertain or important. The cost per QALY under these amended assumptions ranges from £7255 to £18,278. The important conclusion from this sensitivity analysis is that gastric bypass, and surgery in general, seems to produce QALYs at a level that would usually be considered to be cost effective. This result is robust to uncertainty in the model parameters.

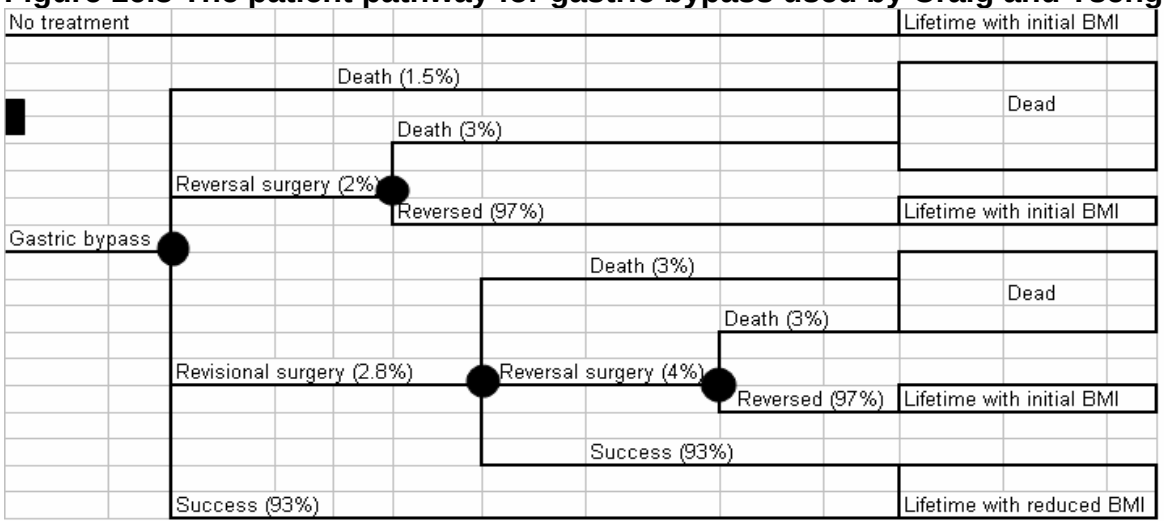
16.6.4 Literature search

The cost-effectiveness literature search for the use of surgery for severe obesity focused on the period following the cut-off in the original report (October 2001). This produced only one study. This study was a cost–utility model, was based in a developed country and had surgery as part of the treatment branch.

[§] SAGB in the figure = ASGB.[DN: change at second draft. Also add commas in numbers [y axis]).

An American study looked at the cost effectiveness of gastric bypass in the treatment of severe obesity.[62] The authors undertook a deterministic decision analysis (Figure 16.3) comparing the lifetime expected costs and benefits from open gastric bypass relative to no treatment. The population group consisted of men and women between 35 and 55 years old, with a BMI between 40 kg/m^2 and 50 kg/m^2, without cardiac disease and who had failed more conservative treatment (such as pharmacotherapy).

Figure 16.3 The patient pathway for gastric bypass used by Craig and Tseng[62]



Costs and benefits were assigned to each of the members of the cohort within each health state. The costs were those of initial surgery, treatment of complications, follow-up care and treatment of obesity-related diseases (CHD, stroke, type 2 diabetes, hypercholesterolaemia and hypertension). QoL was estimated for gender, age and BMI levels from US national statistics. Under their base case, the cost-effectiveness ratios ranged from US$5000 to US$16,100 per QALY for women and from US$10,000 to US$35,600 per QALY for men depending on age and initial BMI (Table 16.32).

Table 16.32 Incremental cost-effectiveness ratios for gastric bypass (Craig and Tseng[62]), stratified by gender and BMI

	Cost per QALY ($)	
BMI (kg/m^2)	**Men**	**Women**
Risk subgroup at age 35 years		
40	28,600	14,700
50	10,700	5,700
Risk subgroup at age 55 years		
40	35,600	16,100
50	13,300	5,400

BMI, body mass index; QALY, quality-adjusted life year.

At face value, these ICERs seem to be promising in favour of the intervention. At current (August 2005) exchange rates, the highest ICER (55-year-old men, BMI of 40 kg/m^2) is £19,900. This would likely be lower since medical costs in the USA tend to exceed those in England and Wales. There is one caveat to this result and this lies in the choice of comparator. In this group of severely obese patients, the alternative to surgery is pharmacology or lifestyle interventions, rather than nothing. The choice of no treatment as the comparator in the study is likely to artificially deflate the cost per QALY.

17 Cost effectiveness of public health interventions

The following is based on work undertaken by the York Health Economics Consortium at the University of York. Detailed evidence tables and supporting information are in Appendix 18.

17.1 Introduction

Obesity is an underlying risk factor for a number of potentially life-threatening diseases, such as coronary heart disease (CHD), diabetes mellitus, and some cancers. For instance, according to the 2001 report by the National Audit Office (NAO), 'Tackling obesity in England', the relative risk of developing type 2 diabetes was 12.7 for obese women and 5.2 for their male counterparts.[63] Consequently, costs arise not only with the direct treatment of obesity but also with the treatment of these associated comorbidities. The NAO has estimated that the costs of treating obesity amounted to £9.5 million in 1998, while the costs of treating consequences associated with obesity equalled the considerably larger figure of £469.9 million. Thus, in total, the burden placed on the National Health Service (NHS) through the treatment of obesity in 1998 was valued at £0.5 billion. This figure is in addition to the indirect costs of £2 billion stemming from productivity losses attributable to obesity.

These substantial, and presumably rising, costs provide overwhelming evidence for the need to implement strategies for the promotion of weight loss, as well as the prevention of weight gain.[64] Treatment options range from changes in lifestyle behaviour or diet to counselling, pharmacotherapy and surgery. This research was commissioned to assess the economics of strategies to prevent obesity through public health interventions. Strategies that can be implemented at a local level, as opposed to national initiatives, were within the scope of the research.

The objective of this work was to assess the cost effectiveness of strategies aimed at preventing individuals from becoming obese. The work was split into two phases:

1. An review of the evidence base on the cost effectiveness of public health interventions to prevent obesity.

2. A modelling exercise.

The modelling exercise was an essential part of this work due to the paucity of data found on cost effectiveness through the evidence reviews.

17.2 Evidence review

17.2.1 Data sources and search strategies

The following information sources were searched:

- Medline
- EMBASE
- Cumulative Index to Nursing and Allied Health Literature (Cinahl)
- Health Management Information Consortium (HMIC)
- Science Citation Index and Social Science Citation Index
- PsycINFO
- Applied Social Sciences Index and Abstracts (ASSIA)
- NHS Economic Evaluation Database (NHS EED)
- Health Economic Evaluation Database (HEED)

The electronic search strategies were developed in Medline and adapted for use with the other information sources.

Parameters for review were as public health review parameters (see Appendix 2). Additional criteria for inclusion were:

- Studies had to have a defined intervention to prevent obesity.
- The study population was not obese at the start of the study (although if drawn from a general population it is accepted that some participants may be obese).

- Studies were included if they reported both the costs and effectiveness of an intervention to prevent obesity (although costs and effectiveness were not necessarily combined into a single cost-effectiveness ratio).
- Studies that only reported the cost of managing obesity in the absence of a well defined intervention or any outcomes data were excluded from the review.

The searches identified 214 potentially relevant references. On the basis of reviewing the title and abstract, 16 full text papers were obtained for further assessment. Once publications had been collated into individual trials and bibliographies checked, the total number of included cohorts was nine. The detailed evidence tables to this review are in Appendix 18.

17.2.2 Results

A total of eight papers were identified which considered the prevention of obesity and included data on cost effectiveness: four randomised controlled trials (RCTs),[65–66], one before-and-after study,[67] one discrete choice experiment,[68] one Markov model[69] and one controlled non-randomised study.[70] No UK studies were identified; studies were carried out in Australia, Denmark, the Netherlands, USA and Canada. The length of follow-up ranged from 16 weeks to 3 years. Overall there was limited information concerning the cost effectiveness of interventions to prevent obesity.

17.2.2.1 Diet and exercise programme

There is some evidence that a diet and physical activity intervention incorporating interactive educational sessions is cost effective when compared with a similar intervention using only mail shot advice for couples living together for the first time.

Dzator and coworkers[65] aimed to investigate the effect a diet and physical activity programme had on Australian couples, living together for the first time. Couples were randomised to a low-level intervention or a high-level intervention or a control group. Patients in the low-level intervention group received an introductory group workshop, followed by mail outs. The high intervention group received mail outs alternated with interactive sessions, with a dietitian and an exercise physiologist. The results show that the intervention was more effective than doing nothing. The high intervention group showed substantial marginal improvement compared to the low intervention

group. This was particularly the case for blood cholesterol, blood pressure, fat intake and fitness. The total cost for the high intervention group was US$41,854.34 (US$445.30 per participant, US$111.33 per month). The total cost for the low intervention group was US$41,847.26 ($445.18 per participant, US$111.30 per month). At 12-month follow-up the total and average incremental costs were US$43,282.10 (US$460.44 per participant, US$38.37 per month) for the high intervention group and US$431,09.43 (US$458.61 per participant, US$38.22 per month) for the low intervention group. The authors report that the high intervention group achieved greater marginal effectiveness and cost effectiveness than the low level intervention. There was no significant difference in BMI at either 4 or 12-month follow up. The average cost of having interactive workshops every 2–3 weeks post-intervention is US$445.50 per unit change in the outcome variable, for the high intervention group, this is US$445.18 for the low intervention group. This shows that the high intervention group costs US$0.12 per participant at the end of the programme and US$1.84 at the 12 months' follow-up, to achieve an additional average unit of improvement (increase or decrease) in the outcomes additional to that achieved in the low intervention group.

Roux and coworkers[68] aimed to assess the cost effectiveness of population wide strategies to promote physical activity in adults. A Markov model was developed to estimate the costs, health gains and cost effectiveness. Efficacy data were taken from randomised controlled trials. A systematic review of disease burden by exercise status was used to obtain the relative risk of five diseases (CHD, ischaemic stroke, colorectal cancer, breast cancer, type 2 diabetes). Four public health strategies that had been strongly recommended by the US Task Force for Preventative Services were investigated. The results show that physical activity access intervention was the most effective intervention but social support was the most cost-effective intervention at US$9000 per quality-adjusted life year (QALY), assuming a 40-year time horizon. All the physical activities were cost effective (with cost-effective ratios ranging from US$9000/QALY to US$30,000/QALY). The results were sensitive to intervention costs and efficacy and analytic time horizon. (Note: the information provided here is taken from an abstract presentation at the North American

Association for the Study of Obesity's (NAASO) 2004 annual conference, and therefore full descriptions were not provided.)

17.2.2.2 Workplace interventions

The evidence did not suggest that physical activity counselling at a workplace resulted in any cost-effective gains in health outcomes and studies on the benefits in terms of lost productivity are equivocal.

Proper and coworkers[71] investigated the cost benefit and cost effectiveness of a workplace physical activity programme among civil servants in three municipal services of a Dutch town. Participants were randomised to an intervention group (n = 94) or control (n = 159). Participants were more likely to be men and of higher education. Participants in the intervention group were offered seven sessions of workplace-based tailored counselling which promoted physical activity and healthy dietary habits. Both the intervention group and the control group received written information about lifestyle factors (physical activity, nutrition, alcohol, smoking, [work] stress) and musculoskeletal symptoms.

The results show that the intervention costs were €430 per participant. There were no statistically significant differences between the total costs or sick leave costs between the two groups. During the intervention the costs due to sick leave were lower in the intervention group, in the year after the intervention the benefits had increased further. During the intervention the mean total costs were higher in the intervention group. The cost-effectiveness results show that improvements in energy expenditure and cardio-respiratory were gained at a higher cost. The authors note that 'due to the very wide (statistically non-significant) confidence intervals, we cannot say with certainty that this is the amount of money to be invested in order to achieve improved energy expenditure and fitness levels'.

Aldana and coworkers[66] investigated the effect the Washoe County School District (WCSD) Wellness Programme had on employee healthcare costs and the rates of absenteeism. Participants were employees and retirees of the WCSD for the years 1997–2002. Participants were eligible if they had been employed full time by the district for 3 or more years, including 2001 and 2002. A total of 6246 were eligible, of

this 1441 were retired. Participants enrolled on line or at any of the different district schools or facilities. Eleven different programmes were offered to all participants, with the programmes being prompted via the internet and email. The programmes addressed weight management, water intake, fruit and vegetables intake, television viewing and various 'exercise' activities. The results show that for every certified and classified employee who was absent from work, on average, the WCSD paid US$231/day and US$103/day, respectively. The cost per day of a substitute employee was US$75. Programme participation was associated with a US$3,041,290 difference in absenteeism cost during 2001 and 2002, when compared with non-participants. This value is '15.6 times greater than the total cost for all wellness programmes during the same time period'. The authors comment that 'these savings translate into a cost saving of US$15.6 for every dollar spent on programming'. Although there were immediate difference in healthcare costs between those who participated and those who did not, there was a significant difference on absenteeism.

17.2.2.3 School-based intervention to reduce obesity

There is some evidence that school-based interventions can result in cost effective health gains. Both interventions identified resulted in weight loss at acceptable costs although the latter is only available in abstract form at present.

Wang and coworkers[72] studied 310 school girls (aged 14 years and under) in the USA, randomised to intervention or the control. The control students received their usual curricula and physical education classes. The intervention group received Planet Health which aimed to infuse the intervention material into the curriculum. The intervention focused on decreasing television viewing, decreasing consumption of high fat foods, increasing fruit and vegetable intake, and increasing moderate and vigorous physical activity. The results show that for the five schools in the study the total intervention cost, over the 2 years, was US$33,677, or US$14 per student. The intervention would lead to 4.1 QALYs being saved. Society would save an estimated US$15,887 in medical costs and US$25,104 in productivity costs. This results in US$4305 per QALY saved and a net saving of US$7313 to society. Sensitivity analysis showed that the cost effectiveness of the programme was relatively

unaffected by changes to most parameters but was more sensitive to changes in the discount rate.

Wang and coworkers[70] investigated the cost effectiveness of an after-school obesity prevention programme, which included third grade students in nine elementary schools. The results show that the cost-effectiveness ratio was US$190 per 1% body fat reduction. For students who attended at least 40% and 80% of the sessions, the programme resulted in an average 0.8% ($p < 0.01$) and 1.2% ($p < 0.01$) body fat reduction, respectively. This was achieved at a cost of US$634 and US$839 per student in after-school care costs. Resulting in a per capita net savings of US$88 and US$293, respectively. The authors concluded that the programme was cost effective and cost saving for students who attended at least 40% of the intervention sessions.

17.2.2.4 Community weight loss programme

There is some evidence that all population-wide strategies to promote physical activity in adults, as identified by the US Task Force for Preventative Services, were cost effective although the outcomes have only been presented in abstract form to date.

Roux and coworkers[69] investigated factors that impact on individuals decisions to adhere to a community weight loss programme by the use of a discrete choice experiment. The study included members of a US-based community weight loss programmes. Participants were 25 years or older with BMI greater than or equal to 25 kg/m^2), had recently enrolled on the scheme, and did not have any comorbidities. The study showed that attributes with a positive coefficient (that is, participants were willing to give up something else to move up a level) were the amount of doctor time, programme components emphasis and the programme focus. Attributes with a negative coefficient (that is, become less preferable as the absolute magnitude of the coefficient rises) were the programme cost for 3 months and one-way travel time. Service attributes do play a marked role in the decisions users of a weight loss programme make. Participants were willing to pay an extra US$600 out of pocket for a 3-month weight loss programme that was more accessible, comprehensive and tailored to the individual when compared with the current available programme.

17.2.2.5 Nutritional counselling

There is some evidence that nutritional counselling by a general practitioner (GP), compared with counselling by a dietitian is cost effective.

Rajgopal and coworkers[67] evaluated the economic efficacy of the Virginia Expanded Food and Nutrition Education Programme (EFNEP) in a controlled before-and-after (CBA) study aiming to improve health and disease prevention. The study was split into three phases:

- investigation of behaviours taught in the EFNEP that might 'contribute to delay or avoidance of diet-related chronic diseases and conditions that are believed to be most prevalent among the low-income population'
- selection of participants from the 3100 graduated homemakers who had met the selected criteria for optimal nutritional behaviour (ONB)
- gleaning data from the previous phases into a CBA formula.

The results show that the initial benefit-cost ratio was US$10.64:$1.00, indicating that for every one dollar spent over 10 dollars may be saved in future healthcare costs. Sensitivity analysis on the initial assumptions and the lack of incidence data for some disease areas gave a benefit-cost ratio ranging from $2.66:$1.00 to $17.04:$1.00:

- On reducing the number of graduates to achieve the optimal behaviours by 75%, the ratio is $2.66:$1.00, and when it is reduced by 50% the ratio is $5.32:$1.00.
- When the portion of osteoporosis due to dietary factors is assumed to be 50%, the ratio is $5.91:$1.00.
- Using only estimated disease incidence rates for low-income populations the ratio is $17.01:$1.00.

It should be noted that this was a general dietary initiative and was not targeted at obesity.

17.2.3 Sub question: variation by gender, age, ethnicity, religious practices or social group

17.2.3.1 Age

From the evidence available this question cannot be answered. No studies were identified that compared outcomes for participants of different ages. There is some evidence to suggest that school-based interventions are cost effective but these studies did not involve comparisons with another age group.

17.2.3.2 Gender

Dzator (2004)[65] investigated the impact diet and physical activity programmes have on couples living together for the first time, the cost-effectiveness analysis was performed on the group as a whole and was not separated out by gender.

17.2.3.3 Social group

In Wang and co-workers'' study of the Planet Health scheme (2003)[72] all the schools involved in the study had a median household income lower than for all the households in Massachusetts, USA. Where the median household income in Massachusetts is US$41,000 and was US$36,020 for the intervention group and US$34,200 ($33,952 for the USA). However, as there were no direct comparisons between different social or income groups no firm conclusions on the relative cost effectiveness of interventions can be drawn.

17.2.4 Limitations of the review

There are only single studies to support each intervention. Although the design of the majority of the studies was of a relatively high standard (that is, RCTs) it is not clear as to whether any of the studies are applicable to the UK. The longest length of follow-up was 3 years; this could affect the generalisability of the results to a longer time period. Based on reviews of the published literature, there is also some difficulty in defining precisely what the interventions involved. Two of the studies[70,70] discussed above are only currently reported in abstract form.

17.3 Economic modelling

17.3.1 Methods

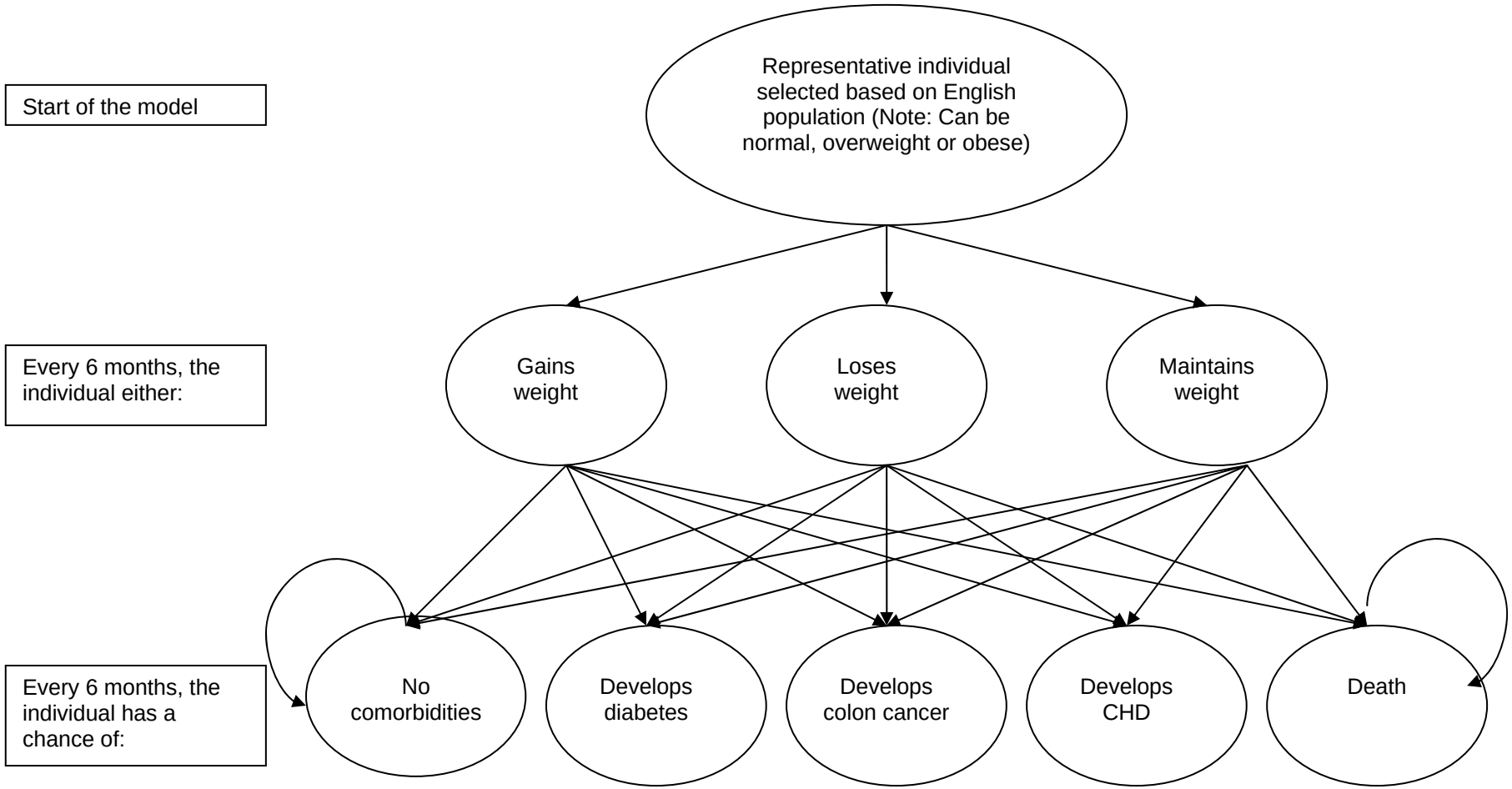
A patient-level simulation model was designed to estimate the costs and QALYs associated with obesity. These costs were compared to the costs and QALYs obtained from three interventions aimed at preventing obesity.

The higher an individual's BMI the more likely they are to develop related co-morbidities, including diabetes, CHD and some forms of cancer. Due to data constraints, the model focused on the increased risk of developing diabetes, CHD and colon cancer. Obesity is recognised as being a risk factor for other conditions, including other cancers, musculoskeletal disease and chronic obstructive pulmonary disease (COPD) however, in the absence of accurate data on these risk factors they are currently excluded from the model. As such, the model provides a conservative estimate of the cost effectiveness of strategies to prevent obesity.

17.3.1.1 The model

The model is defined to assess how a prevention strategy would work in a population that is representative of the population of England as a whole (as data are largely derived from the 'Health survey for England'). The model works by randomly selecting an individual whose characteristics are based on those of the population (for example, BMI, age, gender all determined by population data). Each individual is followed until death and their healthcare costs and outcomes are recorded. This process is repeated 10,000 times to provide a sample population that is broadly reflective of the English population as a whole. It should be noted that the population will include people of 'normal' weight as well as people who are overweight or obese in order to reflect the population of England. This is believed to be an appropriate population to study for a public health intervention. We have not attempted to identify the cost effectiveness of interventions in high-risk subgroups nor have we excluded obese individuals who may be more suitable for treatment than prevention. A schematic diagram of the model is shown in Figure 17.1.

Figure 17.1 Schematic diagram of the model to assess how a prevention strategy would work (CHD, coronary artery disease)



The characteristics of each individual are shown in Table 17.1 below.

Table 17.1 Characteristics of each individual

Characteristics	Parameters	The percentage of people in each group is taken from:
Gender	Male, female	Office for National Statistics[73]
Age (years)	0–16	'Health survey for England 2003'[74]
	16–24	
	25–34	
	35–44	
	45–54	
	55–64	
	65–74	
	75+	
BMI (kg/m^2)	20 or under (not less than 15 if a child, and not less than 18.5 if an adult)	For adults – 'Health survey for England 2003'[74]
	20–25	
	25–30	
	30–40	
		For children – The British Heart Foundation[75] and Cole et al. 2000[76]

The percentage of people in the general population who are male or female and the percentage of people in each of the above age bands are taken from data provided by the Office for National Statistics.[73] The 'Health survey for England 2003'[74] provided the mean BMI for men and women in each age band.

The British Heart Foundation[75] provides the percentage of children who have a 'normal', 'overweight' and 'obese' BMI. Where the definition of 'normal', 'overweight' or 'obese' was taken from Cole and coworkers.[76] The paper focused on children aged between 2 and 18 years, we have assumed that the cut-off points for 2-year-olds are the same for 0- and 1-year-olds. Cole states that the cut-off point for 'normal' BMI is the second BMI percentile. Using BMI charts provided by the Scottish

Intercollegiate Guidelines Network (SIGN)[77] we were able to read off the 'normal' BMI cut-off point. All cut-off points are provided in Table 17.2.

Table 17.2 Cut-off points used in the model

	Boys			Girls		
Age	**Normal**	**Overweight**	**Obese**	**Normal**	**Overweight**	**Obese**
0	14.50	18.41	20.09	14.00	18.02	19.81
1	14.50	18.41	20.09	14.00	18.02	19.81
2	14.50	18.41	20.09	14.00	18.02	19.81
3	14.00	17.89	19.57	13.60	17.56	19.36
4	13.60	17.55	19.29	13.40	17.28	19.29
5	13.40	17.42	19.30	13.00	17.15	19.30
6	13.60	17.55	19.78	13.00	17.34	19.78
7	13.00	17.92	20.63	12.90	17.75	20.63
8	13.20	18.44	21.60	13.00	18.35	21.57
9	13.40	19.10	22.77	13.20	19.07	22.81
10	13.80	19.84	24.00	13.60	19.86	24.11
11	14.00	20.55	25.10	14.00	20.74	25.42
12	14.50	21.22	26.02	15.50	21.68	26.67
13	14.80	21.91	26.84	15.00	22.58	27.76
14	15.20	22.62	27.63	15.40	23.34	28.57
15	15.60	23.29	28.30	16.00	23.94	29.11

Due to data constraints, a simplifying assumption is made when modelling the impact of obesity in children. The model assumes that the only risk factor applicable to children is diabetes and that the increased risk of CHD and cancer only emerges once they are aged more than 16. Although there is emerging evidence on the increased risk of CHD in populations under the age of 16, the data were not felt to be robust enough to include in the model at this point in time. As such, any results in this population should be regarded as conservative estimates of cost effectiveness.

The model assesses people over 6-month cycles over the course of their life. Every 6 months each individual will experience a change in BMI. This will either be an increase, a decrease or no change. The individual can develop diabetes, CHD or colon cancer depending on the prevalence of each disease at the BMI level they are currently experiencing. There is a QALY associated with being at each BMI level and

a QALY associated with each health state defined by the comorbidities. The total cost and outcomes are calculated for the whole cohort.

The strategies for the prevention of obesity were selected by the Guidance Development Group (GDG). These were prioritised based on their relevance to UK practice and also the availability of evidence (although not necessarily conclusive evidence from UK settings) to support them from rapid reviews of their effectiveness. The shortlist considered is:

- **Workplace counselling**: Proper and coworkers[71] investigated the cost benefit and cost effectiveness of a workplace physical activity programme in a Dutch town. Participants in the intervention group were given counselling, which promoted physical activity and healthy dietary habits. Advice offered was tailored to the individual. Both the intervention group and the control group received written information about lifestyle factors (physical activity, nutrition, alcohol, smoking, [work] stress) and musculoskeletal symptoms.

- **Counselling from primary care staff**.

- **Whole-school approach**: Wang and coworkers[72] studied 310 school (aged less than 14) girls in Boston, Massachusetts, USA. The control students received their usual curricula and physical education classes. The intervention group received 'Planet Health' sessions that focused on 'decreasing television viewing, decreasing consumption of high fat foods, increasing fruit and vegetable intake, and increasing moderate and vigorous physical activity'.

    - Family based interventions including the family

      Family programmes lead by health professionals to prevent obesity, improve dietary intake and/or physical activity should provide on-going tailored support and incorporate a range of behaviour change techniques. A number of studies were identified from the clinical reviews which examined this intervention. Whilst all were considered as part of the economic evaluation, only the findings from the study by Israel published in 1985 (referred to in the McLean systematic review[78]) are reported below. The rationale for choosing this particular study is that it is a randomised controlled trial and it provided sufficient detail to allow the intervention to be costed.

A second family-based intervention recommended interventions targeted at children with obese or overweight parents. Whilst this was found to have good quality clinical evidence to recommend its use, it was unfortunately outside of the remit of the economic model. The economic model relies on individuals' characteristics to identify how their weight will progress in the future and how any intervention may impact on future weight gain. However, the individual characteristics considered take no account of the weight of parents. Although the model could be run on a population of children or varying BMI levels, the model is not set up to identify children with obese or overweight parents. Therefore, it was not possible to analyse this recommendation in the economic analysis although some thoughts on the likely cost effectiveness of this intervention are provided in this report.

These strategies impact on the likelihood of an individual gaining or maintaining weight over a given period of time. Ideally, the efficacy of these interventions and their impact on weight maintenance or weight loss would be derived from clinical trials. However, rapid reviews of these interventions were equivocal in their findings with some studies reporting benefits whereas others reported no significant changes. The quality of the research and the reporting of results also meant that deriving data to populate the model from these sources was not always possible. In the absence of data derived from clinical trials, assumptions which are deemed to be reflective of how the intervention may work in the real world have been used. Where assumptions have been used these are clearly stated and have been reviewed by the GDG. Sensitivity analysis has also been conducted to assess the impact of varying any assumptions.

When assessing the cost effectiveness of the prevention strategies the *ceteris paribus* principle, often used in economic modelling, applies which assumes that all other things remain equal. As such, the impact of the interventions is considered in isolation from any other potential positive or negative influences which may be in the environment, such as changes in general awareness of healthy eating, physical activity, etc.

17.3.1.2 Data

Change in weight over time

Fine and coworkers[79] demonstrated that in a population of women aged 46–71 years (mean age 58.5) two-fifths will maintain their weight, two-fifths will gain weight and

one-fifth will lose weight over a 4-year period. It was assumed that these figures would be applicable to the whole population and were used in the model to determine the path of an individual's weight over their lifetime. This approach was adopted as it was perceived as being reflective of how individuals manage their weight in the real world. The alternative approach would be to assume that all individuals gain weight steadily over the course of their lives and have a gradually increasing BMI. Whereas the 'average' individual in the model will steadily gain weight over time, some individuals will maintain a healthy weight over the course of their lifetime in the model. While we accept that this assumed distribution may not be generalisable to the entire population, it is used in the absence of any other source of long-term data.

The net impact of the above distribution is an average increase in weight of 1 kg/year across all individuals (that is, although some individuals will lose weight, some gain weight and some maintain a steady weight, the average individual will gain 1 kg/year). This is consistent with the findings of Heitmann and Garby,[80] who performed a retrospective semi-longitudinal study to determine the pattern of weight changes over 11 years in a Danish population that became overweight in adulthood. To calculate the associated BMI change the average height (from the 'Health survey for England 2003') for each age group and gender was used to calculate the change in BMI for each type of individual.

The relation between BMI and each of the risk factors was derived based on published sources.

The prevalence of diabetes by BMI was taken from a paper by Gregg and co-workers'. [47] These authors used data from several surveys that followed US citizens. In the paper the National Health and Nutrition Examination Survey (NHANES) followed individuals from 1999 to 2000. The results of this survey provided the prevalence of diagnosed and undiagnosed diabetes by BMI level (see Table 17.3) below. These were used to find the prevalence for all BMI levels between 15 kg/m^2 and 40 kg/m^2.

Table 17.3 Prevalence of diagnosed and undiagnosed diabetes

	Diagnosed	Undiagnosed
< 25	0.03	0.011
25–29.9	0.041	0.024

30–34.9	0.067	0.043
> 35	0.151	0.032

Diagnosed cases of diabetes will impact on both the costs and outcomes in the model, whereas undiagnosed cases are only assumed to impact on outcomes as they are assumed to be untreated while undiagnosed.

The prevalence of CHD was calculated using the Framingham equation as set out by Brindle and coworkers.[81] The equation is as follows:

$$\alpha = \exp\left(-0.3155 - 0.2784 * (\mu - 4.4151)\right)$$

where:

$$\mu = \left(15.503 - \left[0.9119 - \log\left(systolic\_blood\_pressure\right)\right] - \left[0.2767 * smoking\right] - \left[0.7181 * \log\left(\frac{total}{high\_density} cholesterol\right)\right] - \left[0.5865 * electrocardiographic\_left\_ventricular\_hypertrophy\right] - \left[1.4792 * \log\left(age\right)\right] - \left[0.1759 * diabetes\right]\right.$$

The variables used in the equation are:

- whether the individual smokes[82]
- systolic blood pressure, of the individual[83]
- total cholesterol (mmol/l), of the individual[84]
- high-density lipoprotein (HDL)-cholesterol (mmol/l), of the individual[85]
- probability of having left ventricular hypertrophy[86]
- whether the individual has diabetes (taken from the model)
- age of the individual (taken from the model).

The above calculation is repeated every 6 months. If the individuals is aged less than or equal to 16 years the prevalence of CHD and cancer is 0 (that is, children can not develop CHD or cancer).

To obtain the prevalence of colon cancer the relative risk of colon cancer for men and women by BMI level[50] was applied to the prevalence of colon cancer in the general population (176 per 100,000 per year[30]) (Table 17.4). The relative risk was assumed to be the same for men and women. This is consistent with a statement by the National Institutes of Health which reported that the relation between colon cancer and obesity may be the same in men and women.[87] It was not possible to stratify the mortality risk associated with colon cancer by age in addition to BMI and sex, so this risk factor remains unadjusted for age.

Table 17.4 Relative risk of colon cancer by body mass index (BMI)

BMI	Relative risk
< 22	1
22–24.9	0.84
25–26.9	1.33
27–28.9	1.62
> 29	1.82

Mortality stratified by age was obtained from interim life tables provided by the Government Actuary's Department.[88] The interim life tables for 2002–04 are based on the mid-year population estimates for 2002, 2003 and 2004. Mortality figures, as used in the model are shown in Appendix 18.

Additional mortality could be due to:

(i) CHD:

- Wood and co-workers' (1994) [89] report that there is no evidence that reducing obesity will have any effect on the mortality from CHD.
- In 2003, a total of 62,400 men and 51,495 women died from CHD.[75]
- A total of 764,800 men and 697,530 women in the UK have CHD.[90]
- This gives a mortality of 8.2% for men and 7.4% for women.
- The relative risk of dying for people with CHD who smoke is 2.9. for men and 3.6 for women.[91]

(ii) Colon cancer:

- The mortality from colon cancer is 14% each year. [51]

Diabetes was not assumed to impact mortality in the model as any deaths attributed to diabetes will be due to complications of the condition rather than diabetes per se.

To determine whether the individual is experiencing each particular health state at any one time, the incidence of diabetes, CHD and colon cancer was calculated. Incidence is calculated from the prevalence using the following equation:

$$Incidence = \frac{\left[\frac{\Pr evalence * percentage\_of\_people\_with\_BMI}{Length\_of\_life\_with\_healthstat e}\right]}{Percentage\_of\_people\_with\_BMI}$$

This equation uses the percentage of people with each BMI, calculated from the data provided by the 'Health survey for England 2003', and the length of life associated with each health state, shown in Table 17.5.

Table 17.5 Length of life

Health state	Age at onset	Length of life	Source
Diabetes	35	33.27	Hoerger et al. 2004[92]
	45	26.20	
	55	18.90	
	65	12.30	
	75	7.28	
CHD (reduction in length of life)		5	Assumed
Colon cancer (reduction in length of life)		5	Based on the fact that 5-year survival is low[93]

17.3.1.3 Effectiveness data

Effectiveness data used in the model were derived from a combination of published studies and assumptions.

For each of the prevention strategies, it was assumed that the prevention would result in weight maintenance for 1 year. This was based on the fact that the majority of clinical studies which had shown any effect on weight were of limited duration and there are few studies which have followed interventions beyond 1 year. As such,

making any assumption about weight maintenance beyond this timeframe would bias the results in favour of the intervention. A we accept that some interventions may have a more lasting effect, in the base case the conservative assumption of 1-year duration is used. This assumption was varied in the scenario analysis to reflect interventions that may have a more lasting impact on weight maintenance.

The efficacy of the prevention strategy relates to the number of people who respond to the prevention. In the base case, it was assumed that the efficacy of each prevention strategy was 75%. The majority of studies reviewed reported efficacy as an aggregated average weight change, rather than achieving a target weight in a given population. However, it seems unreasonable to assume that all individuals will respond to a given intervention so we chose to assume that 75% will respond while 25% will not. The efficacy was varied in during scenario analysis to see its effect on the cost per QALY.

17.3.1.4 Utility weights

Macran[94] provides QALYs by gender and BMI (see Table 17.6). This is the QALY for the general population and not for individuals free from diabetes, CHD and cancer. The unweighted QALY was calculated to correct for this.

Multipliers were applied to this QALY to obtain the QALY for individuals with any of the relevant comorbidities, such as diabetes and CHD. The multipliers for diabetes and CHD were provided by Ara and Brennan (Ara, R and Brennan, A. Economic evaluation of sibutramine for the treatment of obesity in adults without other co-morbidities in the UK. Company submission. 2005) (0.8661 and 0.8670, respectively). Lewis and coworkers[95] reported that the when an individual has colon cancer their QALY is reduce by 5%; this was applied in the model.

Table 17.6 Quality of life by body mass index (BMI) and gender

BMI (kg/m^2)	Male	Female
< 21	0.86	0.85
21–25	0.87	0.87
26–30	0.86	0.82
31–39	0.82	0.78
> 39	0.88	0.75

As such, a man with a BMI of 31–39 who also has CHD, diabetes and colon cancer would have a utility value of 0.58 compared with the 0.82 reported in Table 17.6 for an individual with no comorbidities.

17.3.1.5 Cost data

All costs were converted to January 2005 prices and are presented in Table 17.7. The cost of diabetes and CHD is based on the information provided by Ara and Brennan. (Ara, R and Brennan, A. Economic evaluation of sibutramine for the treatment of obesity in adults without other co-morbidities in the UK. Company submission. 2005) The cost of colon cancer is taken from an Australian paper[96] in the absence of any cost data derived from UK settings. The paper reports the cost of treatment for individuals diagnosed with Duke's A, B, C and D colon cancer. The crude average cost of treatment for these individuals was used in the model. The cost of diabetes was only applied to diagnosed diabetes, where the cost of diabetes includes:

- two GP visits
- one specialist nurse visit
- two visits to a GP clinic
- one HbA1c test
- 12 home glucose tests
- half an eye screening
- blood pressure control using angiotensin-converting enzyme inhibitor – ramipril
- a diuretic
- statin therapy (simvastatin)
- metformin antiglycaemic therapy.

No costs were included for undiagnosed diabetes as these individuals are assumed not to present to a healthcare professional and as such do not represent a burden to the NHS. However, the losses in utility related to undiagnosed diabetes cases was

included in the model as these would occur regardless of whether the case was diagnosed or treated.

Table 17.7 Costs per patient per year (as January 2005 prices)

Annual cost	Cost, as reported in paper	2005 UK cost	Source
Diabetes cost components	£633	£653	a
Coronary heart disease	£1587	£1637	a
Colon cancer	Aus$18,435	£7320	O'Leary 2004[52]
Workplace counselling	€430	£296	Proper et al. 2004[71]
Counselling from primary care staff (a year)	–	£728	This is assumed to be the cost of half an hour of practice nurse time, once a week[97]
Whole-school approach (per child)	$14	£12	Cost converted to UK £ and inflated to 2005 prices[72]

[a] Ara, R and Brennan, A. Economic evaluation of sibutramine for the treatment of obesity in adults without other co-morbidities in the UK. Company submission. 2005.

17.3.1.6 Economic evaluation

Incremental cost effectiveness was performed for the base case compared to each intervention. Cost-effectiveness models are used to assess the relative benefits of a given treatment using patient outcomes and the costs incurred in achieving those outcomes. The calculation of the additional cost per additional unit gain of benefit is known as the incremental analysis and results are presented as incremental cost-effectiveness ratios (ICERs).

After incremental costs and QALYs were estimated, the ICERs were calculated using the following formula:

$$ICER = \frac{Cost_{prevention} - Cost_{base\_case}}{Effect_{prevention} - Effect_{base\_case}}$$

17.3.1.7 Scenario analysis

The base case for each of the strategies reviewed was assumed to be weight maintenance (that is, no change in weight), over a 1-year period, after which

individuals would revert to the normal weight trend in the underlying model. The efficacy of each of the interventions was assumed to be 75%.

Due to uncertainty around the assumptions used in the prevention strategies, a number of scenarios were run for each prevention (using a cohort of 10,000). These scenarios were intended to capture best and worst case scenarios as well as a number of scenarios that may be feasible but are currently not supported by long-term evidence. These scenarios are shown in Table 17.8.

Table 17.8 Scenario analysis

	Scenario				
	1	**2**	**3**	**4**	**5**
Weight change (kg)	0	0	0	0	–10
Time (years)	20	40	90	1	2
Time to regain weight where loss occurs (years)	0	0	0	0	2
Efficacy (%)	75	75	75	100	75
Cost (time costs are applied)	1	1	As in the base case[a]	As in the base case[a]	As in the base case[a]

[a] The costs for work place counselling are applied for 1 year, the costs for primary care for half a year and the costs for the whole-school approach for 2 years.

The scenarios used allow the duration of weight maintenance to be changed from the 1 year used in the base case. Longer episodes of effect are allowed to model the best case scenario whereby public health interventions have a lasting impact on lifestyle and weight maintenance. The duration of effect has been varied from 1 year to 20 years, to 40 years and finally to a lifetime effect (90 years captures the entire duration of the model and the individuals within it). In addition to this, we have varied the efficacy from our assumption of 75–100% to determine the impact on outcomes and also varied the weight maintenance assumption. In one scenario we have assumed that the prevention strategy results in weight loss of 10 kg over a 2-year period which is then regained over the following 2 years.

17.3.2 Results

In this section the costs and QALYs for the prevention strategies compared with a 'do nothing' strategy are presented. It should be emphasised that 'do nothing' means that no additional active interventions are established but normal care continues. In the prevention arms, the prevention strategies are assumed to be in addition to ongoing normal care. Incremental analysis is presented in Table 17.9. These results are followed by the scenario analysis.

17.3.2.1 Base case results

Table 17.9 presents the results of the base case analysis. The base case assumes that weight is maintained over 1 year, and that all preventions have an efficacy of 75%.

Table 17.9 Base case analysis

Prevention	Prevention				Do nothing			
	Costs	SD	QALY	SD	Costs	SD	QALY	SD
Work place counselling	£2,072.16	£5,451.83	28.24	12.62	£1,810.67	£4,794.02	28.15	12.65
Counselling from primary care staff	£2,148.65	£5,220.63	28.12	12.66	£1,842.26	£5,234.97	27.99	12.79
Whole-school approach	£1,817.48	£5,011.64	28.19	12.74	£1,810.89	£5,131.78	28.17	12.76
Family-based intervention	£2,233.17	£5420.55	28.38	12.60	£1807.72	£4820.34	28.15	12.61

QALY, quality-adjusted life year; SD, standard deviation.

The results show that all the prevention strategies result in more QALYs than the 'do nothing' model. Over a lifetime the average cost of the prevention strategy is more expensive than doing nothing which is to be expected.

Figures 17.2–17.5 present graphs of BMI plotted over time for the first 10 years for all the prevention strategies. The graphs show that during the first year of the model BMI is marginally reduced compared with the underlying trend in weight gain and then gradually increases for the next 9 years. BMI for the prevention stays below BMI for the 'do nothing' model and for the most part runs parallel.

During the first year the BMI line for the prevention is not horizontal. This is because:

- the efficacy is only 75% (that is, 25% of individuals are assumed to not respond to the intervention and do not maintain their weight);
- each prevention may only be given to some of the population, with:
    - workplace counselling being given to adults only
    - counselling by primary care staff being given to both adults and children
    - whole-school approach only being given to children.

Figure 17.2 Work place counselling – body mass index (BMI [kg/m^2]) over time

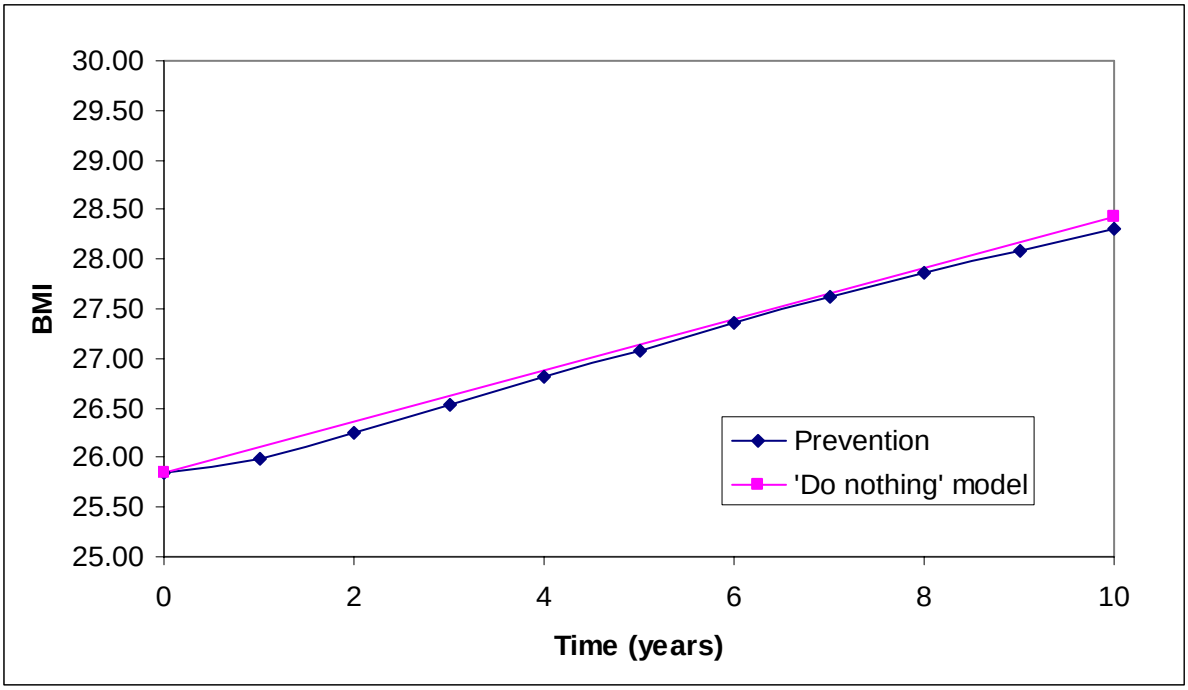


Figure 17.3 Counselling by primary care staff – body mass index (BMI [kg/m^2]) over time

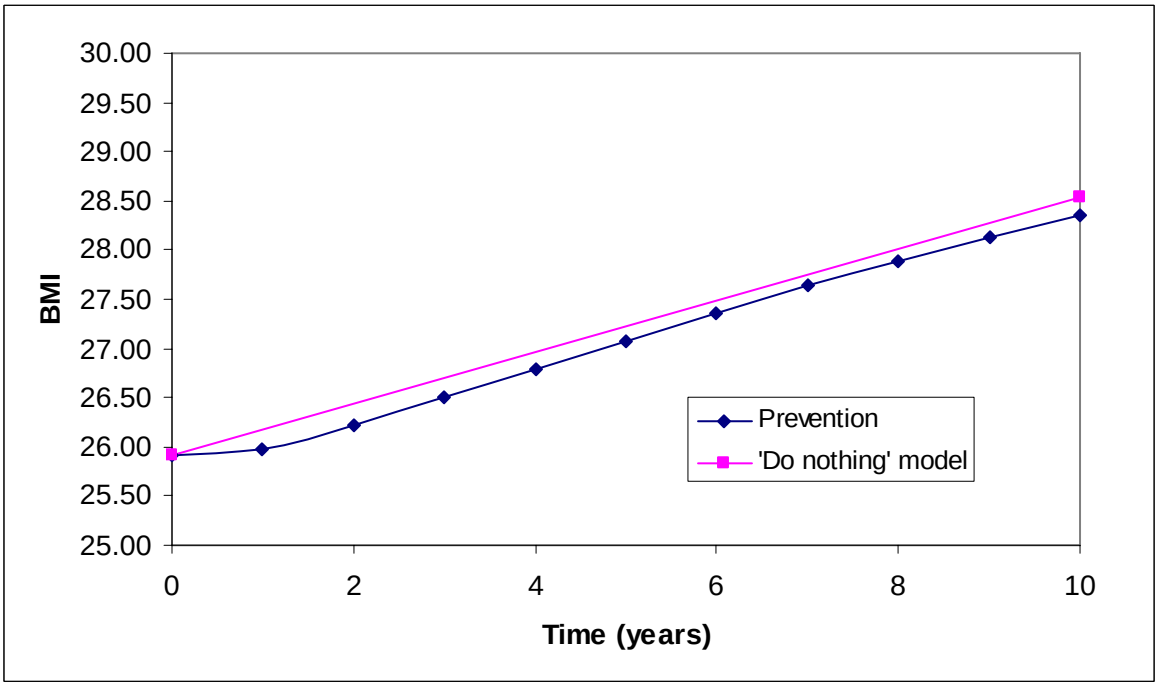


Figure 17.4 Whole school approach – body mass index (BMI [kg/m^2]) over time

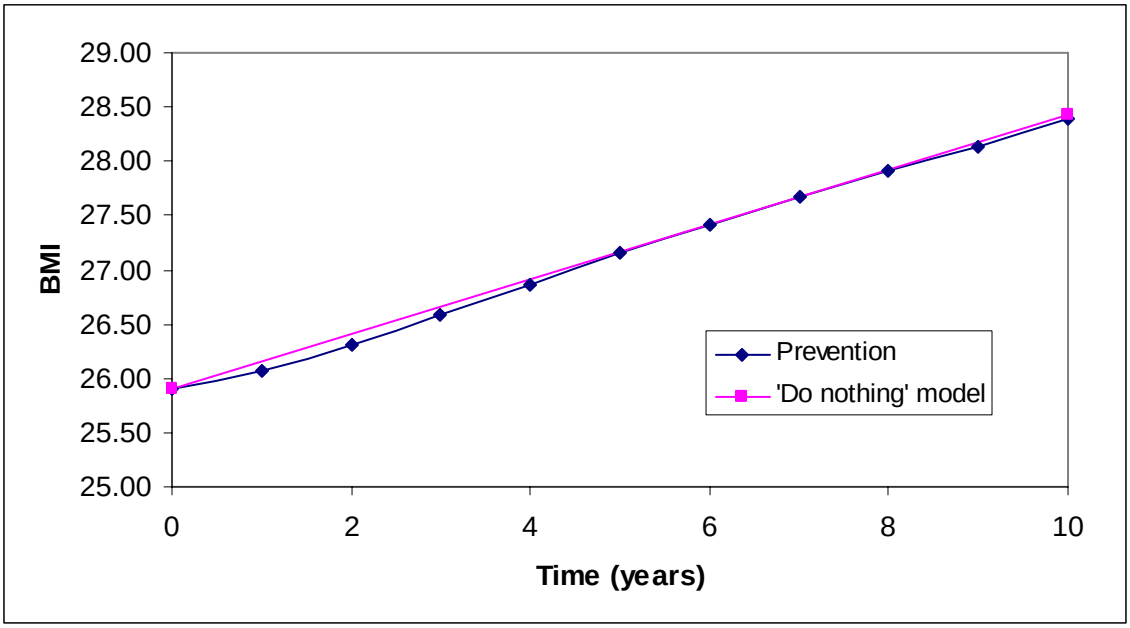
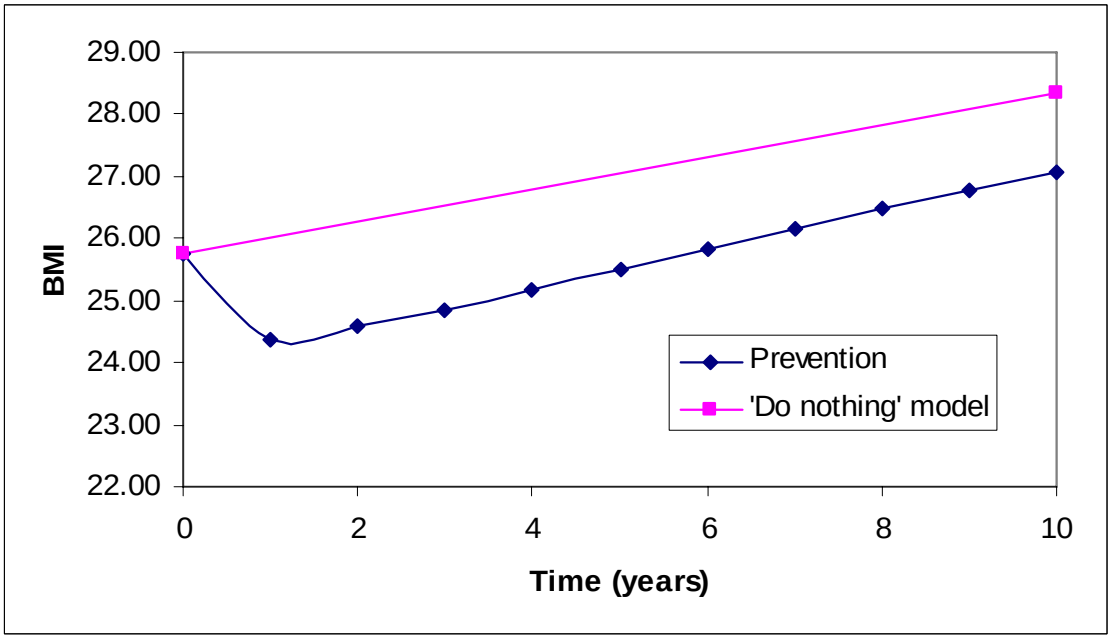


Figure 17.5 **Family-based interventions, BMI over time**



17.3.2.2 Incremental analysis

The incremental results are presented in Table 17.10 below. These results show that all the approaches produce a relatively low incremental cost per QALY which is well within accepted ranges. Although this is positive, it should be noted that the ICER is low as a result of low intervention costs and low QALY gains. The QALY gains in

particular are low and close to 0 in some cases. Further explanation of this is included in the discussion (section 17.3.3).

Table 17.10 Workplace counselling

	Incremental cost	Incremental QALY	ICER
Workplace counselling	£261.49	0.087	£3018.31
Counselling by primary care staff	£306.39	0.132	£2313.51
Whole-school approach	£6.59	0.025	£265.98
Family-based interventions	£425.16	0.23	£1,826.13

ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Although it was not possible to assess the cost effectiveness of family based interventions that target children with overweight/obese parents, there is no reason to suggest that this would differ substantially from the above results. Indeed, it could be argued that targeting an intervention to children with an increased risk of weight gain may result in the intervention being even more cost effective than interventions which are aimed at a general population.

17.3.2.3 Scenario analysis

The results of the scenario analysis are shown in Table 17.11.

As the analysis of family-based interventions was run at a later stage based on the recommendations of the Guideline Development Group, the scenario analyses have not been run on this intervention.

Table 17.11 Scenarios analysis for workplace counselling

Scenario	Workplace counselling			Counselling by primary care staff			Whole-school approach		
	Incremental cost	Incremental QALY	ICER	Incremental cost	Incremental QALY	ICER	Incremental cost	Incremental QALY	ICER
1	£247.36	0.222	£1113.38	£715.25	0.393	£1818.87	-£33.71	0.117	Dominant
2	£269.39	0.213	£1264.56	£451.28	0.439	£1027.66	-£103.40	0.282	Dominant
3	£287.44	0.214	£1345.29	£201.46	0.483	£416.97	£26.28	0.163	£161.44
4	£150.52	0.012	£12154.42	£430.80	0.008	£55320.01	£47.32	-0.018	-£2600.74
5	£167.96	0.170	£987.35	£258.29	0.118	£2190.50	£27.14	0.026	£1035.60

ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Each of the scenarios used in the sensitivity analysis was defined to address extreme values of a single parameter or changes to a number of parameters.

17.3.2.4 Sensitivity analysis of duration of weight maintenance/loss

Scenarios 1, 2 and 3 model the impact of extending the duration of weight maintenance from 1 year in the base case to 20 years, 40 years and 90 years, respectively. Given that costs are accrued over a single year and benefits accrue long into the future, it is not surprising that these scenarios produce cost-effective outcomes. The QALY gains should be expected to increase under each of the scenarios. Whereas this is true in the case of primary care counselling, the gains are less consistent for workplace counselling and school-based interventions. One explanation of this is that primary care counselling is the only intervention assumed to benefit the entire population, whereas workplace and school-based interventions benefit only a sub group of the population. As such, benefits will accrue in these groups over time but may decrease in the long term as members of these subgroups die.

Under each of these scenarios the QALY gains are significantly greater than those of the base case suggesting that the duration of the impact of an intervention is an important factor from an economic perspective.

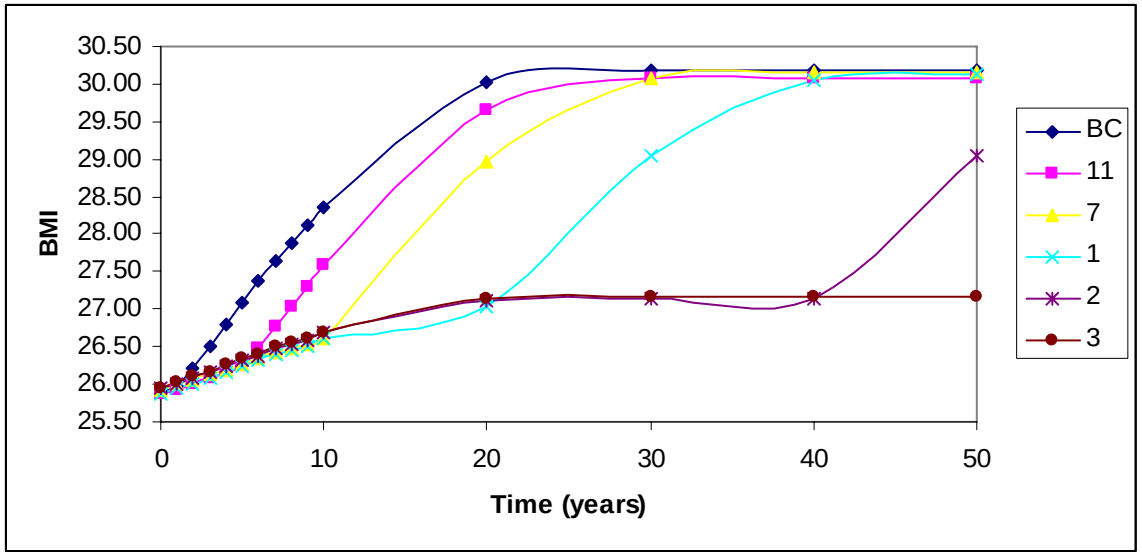
Further analysis was carried out to see whether the pattern of increasing QALY and decreasing cost per QALY would be seen when the duration of weight maintenance was one, five and ten years. The counselling by primary care staff model was rerun; this scenario was chosen because it targets the whole population. Table 17.12 provides the results; the duration of weight maintenance modelled by each scenario is recorded in the table. These results clearly show that the incremental QALYS gradually increase, and that on the whole the ICERS gradually decrease, as the duration of weight maintenance increases. Figure 17.5 plot BMI over time for all the scenarios as would be expected.

Table 17.12: Further analysis, duration of weight maintenance

Scenario	Time (years)	Incremental cost	Incremental QALY	ICER
BC	1	£306.39	0.13	£2,313.51
11	5	£174.54	0.21	£825.45
7	10	£401.85	0.28	£1,439.55
1 [a]	20	£715.25	0.39	£1,818.87
2 [a]	40	£451.28	0.44	£1,027.66
3	90	£201.46	0.48	£416.97

[a] Costs are over one year not .5 of a year as in the base case.

Figure 17.5 Counselling by primary care staff – increasing the duration of weight maintenance



17.3.2.5 Sensitivity analysis of amount of weight maintenance/loss

Under scenario 5 the intervention leads to an assumed weight loss of 10 kg over the course of 2 years which is then regained over the following 2 years. All of the interventions showed small QALY gains under this scenario similar to those of the base case.

17.3.2.6 Sensitivity analysis of the efficacy of the interventions

Under scenario 4, weight is maintained for 1 year as in the base case but the efficacy of the interventions is increased to 100%. Under this scenario the QALY gains are close to 0 or negative in some cases which increases the cost-effective ratios. One would expect the outcome to be more cost effective than the base case so these results may be a statistical anomaly.

Graphs of BMI over time for all scenarios compared with the base case for each of the preventions and each of the corresponding 'do nothing' models are shown in Appendix 18.

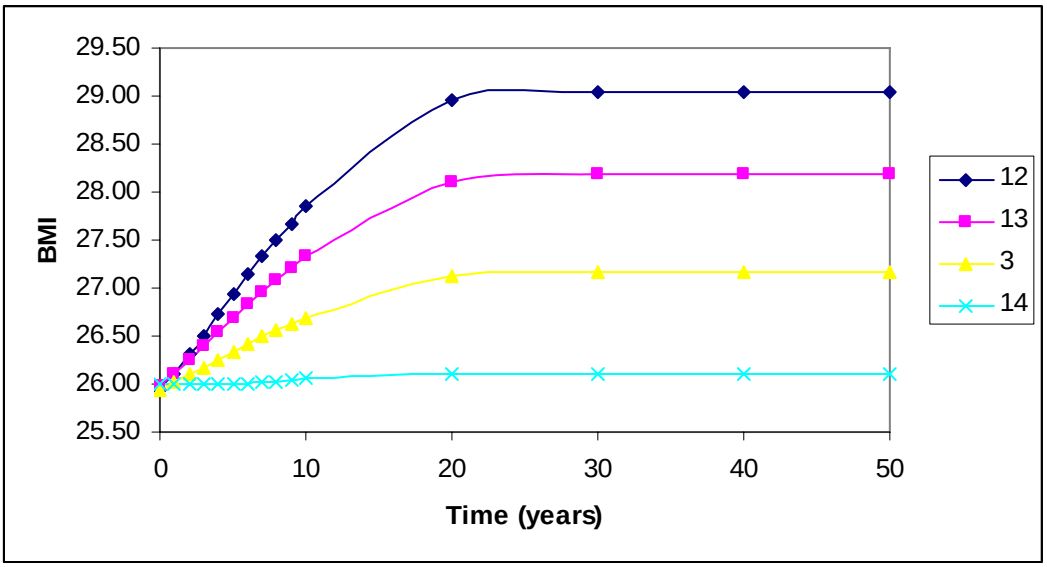
Further analysis was carried out to see whether, when weight is maintained for 90 years, and the efficacy is increased from 25% to 100% the results become more cost-effective. Whilst it is accepted that this duration of effect represents an extreme analysis, this approach was used to ensure that the model was producing logical findings. The use of extreme inputs should ensure that the ICER follows a downward trajectory as efficacy is increased. Given the relatively small impact that a 1 year intervention has on lifetime QALYs, interventions which a short duration may show a less consistent trend. Again the counselling by primary care staff model was run.

The results are presented in Table 17.13 and show that as the efficacy is increased the scenario becomes more cost-effective as would be expected. Figure 17.6 plots BMI over time for these scenarios.

Table 17.13: Further analysis, efficacy of the intervention

Scenario	Time (years)	Efficacy	Incremental cost	Incremental QALY	ICER
12	90	25	£194.77	0.04	£5,343.32
13	90	50	£233.74	0.27	£857.96
3	90	75	£201.46	0.48	£416.97
14	90	100	£213.24	0.67	£318.57

Figure 17.6 Counselling by primary care staff – increasing the efficacy



17.3.3 Discussion

17.3.3.1 Main results and key drivers

The model evaluates the incremental cost effectiveness of a number of obesity prevention strategies. The costs for each of the strategies have been based on published sources of assumptions of the resource use involved and are believed to be robust. Due to an absence of robust clinical evidence derived from long-term studies relevant to UK settings, we have assessed the cost effectiveness of the interventions using a number of scenarios. In the base case, interventions are assumed to be 75% efficacious (that is, three=quarters of people respond to them) and result in weight maintenance over the course of 1 year. The results of the base case analysis show that all the interventions produce marginal QALY gains at a relatively low cost per person. Targeting children appears to be the most cost-effective prevention strategy under these assumptions.

However, it should be noted that although the ICER is low, this arises because both the incremental cost and the incremental QALY gains are relatively low. In

the base case, the QALY gains are marginal and close to zero in some cases, suggesting that short-term weight maintenance does not have a significant long-term impact on health. The reason for this is that the prevention strategies have only a short-term impact on BMI. When this is multiplied by the probability of developing any risk factors in the average individual in the population (as opposed to a high-risk or obese individual), the QALY gains over the course of a lifetime are relatively small. When the trends in weight are mapped, it becomes apparent that both the 'do nothing' and the prevention group's weight continues to increase (reflecting the underlying trend for weight gain and an efficacy less than 100% in the prevention strategies) until the average BMI of both populations plateaus at around 30 kg/m^2. This is because we have assumed that when BMI reaches 40 kg/m^2 it can not increase any further. Any gains from reductions in mortality are minimal as the majority of people in the model die from old age as opposed to one of the predefined risk factors.

The impact of this is shown graphically in Figure 17.5, which shows the costs and benefits of the 10,000 individuals that are sampled in the model. In this case, the costs and benefits associated with primary care counselling produced by the model are distributed around the origin. As such, for each individual who is predicted to have QALY gains there are almost as many who have QALY losses. The net impact is close to zero.

Figure 17.5 Incremental quality-adjusted life years (QALYs) against the incremental costs – counselling by primary care staff

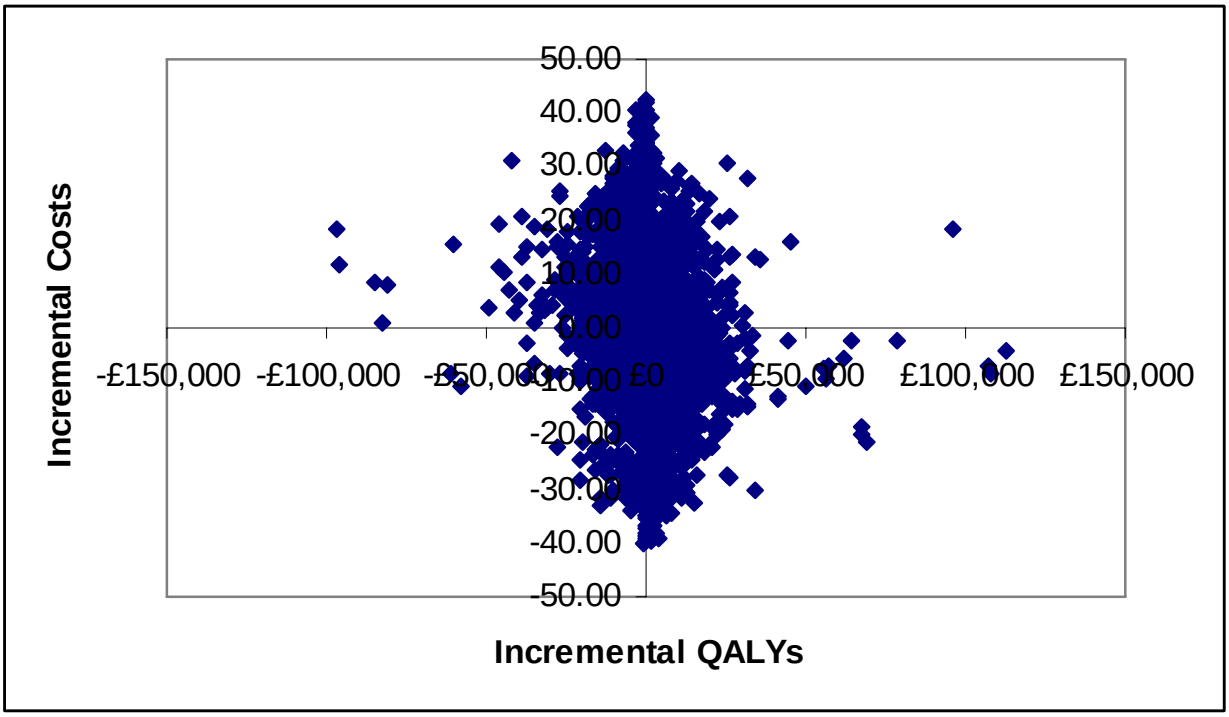


Figure 17.5 shows that the incremental QALYs are concentrated around zero and helps to demonstrate why the average incremental QALYs are so low.

Of the interventions considered in this analysis, there is little reason to suggest that any particular intervention is more cost effective than the others. The results of the base case and the scenarios run above do not lead to a consistent outcome across all scenarios. However, it does appear that the QALY gains resulting from the whole-school approach tend to be slightly lower than the other two interventions. This may reflect the fact that this intervention only benefits a subgroup of the total population assessed (for example, children) and as such has a relatively moderate impact across the total population in the model. In addition to this, the assumption in the model that diabetes is the only risk factor that is applied to children under the age of 16 (that is, we exclude any risk of CHD or cancer until after this age) may also result in underestimates of the QALY gains in this population. However, this needs to be balanced against the

lower costs associated with the whole school intervention which produces a relatively low cost effectiveness ratio.

In general it would appear that strategies to prevent obesity are broadly cost-effective although the QALY gains are low in some cases but these are offset by the low costs of the interventions. The key to improving the cost-effectiveness of such interventions is to ensure that the interventions have a lasting effect on weight maintenance or result in weight gain. Whilst interventions that have only a short-term impact on weight gain may result in some initial improvements in outcomes, these are unlikely to translate into longer-term gains in quality adjusted life-years when considered over the course of an individual's life. Therefore, from an economic perspective, interventions to prevent obesity should look to reduce or maintain weight with ongoing follow-up to ensure that any effect is long-lasting.

It should also be noted that the quality of the clinical evidence underlying the economic evaluation was relatively poor, hence the use of extensive scenario analysis to determine the cost effectiveness of the interventions under different assumptions. The scenario analysis suggests that the interventions under consideration are cost effective under a wide range of assumptions. However, improvements in the reporting of clinical studies in this field would allow for a more robust economic evaluation.

17.3.3.2 Sensitivity analysis

The model is sensitive to changes in the duration of effect. For example, under scenario 2, we assumed that a 1-year intervention leads to a 40-year impact on weight maintenance. Although this scenario is based on extreme values, it could be seen to reflect an educational campaign that leads to a long-term impact on weight management. In this case the cost-effectiveness ratio is consistently low across all the prevention strategies suggesting that the duration of effect of interventions is a key determinant of the cost effectiveness. As such, studies

should attempt to capture long-term outcomes resulting from short-term prevention strategies.

The model is largely insensitive to whether the intervention results in weight maintenance or weight loss. One of the reasons for this is that weight loss is assumed to be temporary and that individuals 'rebound,' putting the weight back on over a period of time.

Although changes in efficacy had an inconsistent impact in the modelling exercise, this parameter does need to be clearly reported in clinical trials of prevention strategies. Studies should clearly define the criteria for response to an intervention and ensure that the results are reported transparently. All too often, studies report outcomes such as average weight loss across a study sample, rather than reporting the proportion of individuals that lost weight and their weight loss. Such reporting would help with future economic studies.

17.3.3.3 Limitations of the model

There are a number of limitations to the model which need to be highlighted. These limitations were mainly put in place due to the absence of accurate data or the computational complexity of the modelling exercise. In line with the best practice in modelling, any simplifying assumptions have erred on the conservative side, so as not to add favourable bias to the study outcomes.

The model occasionally provides unpredictable outcomes which are unexpected, for example, smaller QALY gains when a lifetime (90-year) duration of effect is assumed that a 40-year duration of effect. Some of these can be explained by interventions that target particular subgroups, but some differences remain unexplained. In examining the prevalence of particular conditions in the model it becomes apparent that the QALY gains are easily influenced by a small number of individuals who have multiple comorbidities. For example, if a small number of hypothetical individuals in the sample of 10,000 used in the model develop diabetes, CHD and colon cancer or experience premature mortality, this reduces QALY gains in the whole cohort significantly. Running the model for a sample of

10,000 individuals would normally overcome these sort of inconsistencies. However, due to the relatively small reductions in risk and the resulting increases in QALYs that occur from weight maintenance, these 'outliers' can impact the ICERs and in some cases result in small QALY losses in the prevention group. This may be overcome by running even larger samples in the model, but this would increase the computational burden of an already complicated model. In order to ensure that these instances are a true statistical anomaly, a number of extreme scenarios have been run, such as assuming that interventions have a 90 year effect but a variable efficacy from 25% to 100%. These extreme scenarios have produced logical changes in the ICER that would be expected (e.g. increasing ICER when effectiveness or amount of weight lost is decreased). This testing of the model suggests that the variability in the findings mentioned above arises from the limited impact of short-term interventions on lifetime outcomes and costs rather than any shortcomings in the model structure.

The model only takes into account three key risk factors arising from obesity, namely diabetes, CHD and colon cancer. However, there is limited evidence suggesting that obesity has the potential to increase the risk of other cancers, musculoskeletal disease as well as respiratory conditions such as chronic obstructive pulmonary disease. These were excluded from the model due to the limited information available to accurately predict the increased risk of acquiring any of these conditions based on an individual's age, sex and BMI. As such, any estimates of QALY gains resulting from the model should be regarded as conservative assumptions as they are not assumed to impact on any of these other factors. The relative risks of death associated with the risk factors has also not been age adjusted in the case of colon cancer, which could also reduce the QALY gains that may result from any prevention strategy which impacts this condition.

Another limitation of the model that applies only to children is the assumption that children are only at an increased risk of developing diabetes as a result of being overweight or obese. Once again, due to limitations of the data that are available,

we have assumed that the risks of CHD and colon cancer do not increase until the individual is aged over 16 years. This may result in underestimates of the QALY gains in children.

An additional point for consideration is that the model only captures direct costs (that is, those which fall on the NHS). Once again, this is a conservative assumption as many of the costs associated with obesity may fall on individuals as well as society more broadly. However, for the purposes of this exercise these have not been considered.

In addition to the above structural limitations of the model, there were also limitations due to the lack of data concerning the prevention strategies considered. In the available clinical literature (as identified by the accompanying rapid reviews) many studies reported incomplete costs and benefits resulting from an intervention. For example, many studies reported aggregated results of weight loss or changes in BMI over a study period but did not provide sufficiently disaggregated data on the efficacy of interventions (that is, how many people responded) or the average weight loss in particular subgroups. All studies reviewed were of relatively short duration meaning the duration of effect could not be reported accurately. As shown in the scenario analysis above, this is a key determinant of the cost effectiveness. There were also significant concerns over the use of data from non-UK settings and how applicable these would be to a UK population.

In order to overcome this, a number of scenarios were modelled to assess the likely cost effectiveness of the interventions. The costs of each intervention were based on published sources or assumptions of practice patterns. The base case assumptions took a conservative perspective of the likely impact of interventions, assuming that they were effective in 75% of all participants and that weight loss was managed for 1 year. This was chosen as a realistic assumption as not all individuals would be expected to respond to an intervention and what evidence

there is available did not report any weight maintenance outcomes beyond 1 year.

In the sensitivity analysis, a number of scenarios were developed to reflect more extreme values as well as scenarios which reflected particular behaviours seen in clinical data (for example, the assumption that any weight loss is regained over a period of time following an intervention). These scenarios helped to identify the parameters that are most sensitive to change.

Other authors who have investigated strategies to prevent obesity are Avenell and coworkers[98] and the Health Development Agency.[99] Both studies faced problems similar to this research and were confronted by the lack of appropriate data to support their modelling exercises. Avenell used a Markov model to estimate the cost effectiveness of lifestyle treatments for obesity. The model looked at the effectiveness of lifestyle interventions on preventing the onset of diabetes among people with impaired glucose intolerance. Diet and exercise were compared with no intervention, the ICER or cost per additional QALY was £13,389 at 6 years' follow-up. In 2003 the Health Development Agency report on the management of obesity and overweight found there is an urgent need for more evidence concerning the prevention of obesity and weight maintenance.[99]

17.3.4 Conclusions

The interventions to prevent obesity included in this assessment appear to be a cost-effective use of resources. The cost effectiveness of the interventions is dependent on the duration of effect as well as the extent of any weight loss, suggesting that interventions such as education or counselling should be designed to ensure that they have a lasting effect on individuals' behaviour and weight management, ideally over the course of their lifetime. The clinical literature on the effectiveness of the interventions reviewed was equivocal in some cases which lead to the use of extensive scenario analysis. Whilst the scenario analysis has shown the interventions to be cost effective under a wide-range of assumptions, it would be preferable to have access to clinical studies

that report detailed information on the impact of interventions and include long-term follow-up to support future economic evaluations.

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