

# Is doctor referral to a low energy total diet replacement programme cost-effective for the routine treatment of obesity?

## Running title

Cost-effectiveness of total diet replacement

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## Keywords

Overweight, obesity, primary care, drugs, cost effectiveness

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## Word count

3608

## **Funding**

Funding for this study was provided through a research grant from Cambridge Weight Plan UK Ltd to the University of Oxford and also supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care Oxford at Oxford Health NHS Foundation Trust. All authors are supported by the Oxford NIHR Biomedical Research Centre and SAJ and PA are also NIHR senior investigators.

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The views are those expressed by the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. The University of Oxford holds the relevant clinical trials insurance policy for this study and acted as the study sponsor.

## **Disclosures**

Funding was received from Cambridge Weight Plan UK Ltd to undertake this research. The authors declared no conflict of interest.

## **Author contributions**

SAJ and PA designed the DROPLET study, and NA was the trial manager. SK and BM designed the cost-effectiveness analysis. SK led the cost-effectiveness analysis and wrote the first draft of the manuscript. All authors contributed to the interpretation of the data, the critical review of the manuscript and approved its final version.

### **What is already known about this subject?**

- Total diet replacement (TDR) is an effective method for weight loss in routine healthcare settings
- In the DROPLET randomised trial, doctor referral to a low energy TDR programme reduced weight by an additional 7.2 kg at 12 months in comparison to a nurse-led behavioural support programme
- National guidelines in the UK and the US do not recommend TDR programmes for routine treatment of obesity

### **What does this study add?**

- This is the first cost-effectiveness analysis of a TDR programme for the routine treatment of obesity.
- TDR is projected to be cost-effective at current retail prices under plausible scenarios about weight regain after 12 months

## **ABSTRACT**

### **Objective**

To estimate the cost-effectiveness of a commercially provided low energy total diet replacement (TDR) programme versus nurse-led behavioural support.

### **Methods**

We used a multi-state lifetable model and the weight reduction observed in a randomised controlled trial to evaluate the quality-adjusted life-years (QALYs) and direct healthcare costs (in UK 2017 prices) over a lifetime with TDR versus nurse-led support in adults who were obese, assuming that: i) weight returns to baseline over 5 years, and ii) a 1 kg weight loss is maintained after 5 years following TDR.

### **Results**

The per-person costs of the TDR and nurse-led programmes were £796 and £34, respectively. The incremental cost-effectiveness ratio (ICER) of TDR was £12,955 (95% confidence interval: £8,082 to £17,827) assuming all weight lost is regained and £3,203 (£2,580 to £3,825) assuming that a 1 kg weight loss is maintained after 5 years. TDR was estimated to be more cost-effective (i.e. lower ICERs) in older adults and those with higher body mass index, with little difference by gender.

### **Conclusions**

At current retail prices and with plausible long-term weight regain trajectories, TDR is projected to be cost-effective in obese adults and could be considered as an option to treat obesity in routine healthcare settings.

## INTRODUCTION

Obesity is a common condition [1] which is associated with higher risks of type-2 diabetes, vascular disease, osteoarthritis, and some cancers, among other conditions [2]. As a consequence, it accounts for a substantial share of healthcare expenditure. A recent systematic review reported that adults with obesity incurred, on average, a third higher total annual healthcare expenditures than healthy weight adults [3]. Weight loss achieved with lifestyle interventions has been shown to reduce all-cause mortality [4], diabetes incidence [5], and cardiovascular risk factors [6].

Multicomponent behavioural interventions have been shown to reduce weight by about 2 kg compared with control at 12 months [7], and have been estimated to be highly cost-effective [8, 9]. Very-low-energy diets (providing <800kcal/d) together with behavioural programmes reduced weight by an additional 4 kg at 12 months compared to intensive specialist-delivered behavioural programmes alone [10]. However, national guidelines do not recommend them for routine treatment of obesity [11, 12].

Total diet replacements (TDR) programmes involve the replacement of foods with specially formulated, nutritionally-complete products. Two recent trials have shown that similar TDR programmes, providing 810-850 kcal/d, together with behavioural support from a health professional or trained counsellor, led to comparable weight losses in routine healthcare settings [13, 14]. Although substantially more effective than behavioural interventions alone, TDR programmes are typically more costly, and their cost-effectiveness is not known.

In this study we evaluate the long-term effects and cost-effectiveness of doctor referral of adults with obesity to a commercially provided low-energy TDR programme (Cambridge Weight Plan) using the DROPLET study results [14, 15].

## **METHODS**

### **The DROPLET trial**

A detailed description of the DROPLET trial is presented elsewhere [15]. In brief, 278 adults with a BMI  $>30$  kg/m<sup>2</sup>, identified through primary care registers, were recruited into the study. Participants were randomly allocated either a behavioural support programme delivered by their practice nurse or a low energy total diet replacement (TDR) programme offered by a commercial provider, with products comprising an initial 810 kcal/d for 8 weeks, followed by gradual food reintroduction for 4 weeks, and a further 12 weeks follow-up, along with regular behavioural support (15 sessions over 24 weeks). Both programmes were delivered at no cost to participants.

272 participants contributed data on clinical outcomes (6/278 participants withdrew their consent for use of data). These participants were predominantly female (61%), aged from 19 to 78 years with a mean age of 47 years (standard deviation [SD] 13) in men and 50 years (SD 13) in women, and with a mean body mass index (BMI) of 37.2 kg/m<sup>2</sup> (SD 5.4 kg/m<sup>2</sup>) [14]. At recruitment, 23% had a diagnosis of hypertension and 15% had type-2 diabetes; 30% were taking medication for diabetes or hypertension.

At 12 months, participants allocated the nurse-led behavioural support programme had lost, on average, 3.1 kg (SD 7.0 kg), while those allocated TDR lost 10.7 kg (SD 9.6 kg). In an intention to treat analysis, adjusting for age, sex, and baseline stratification variables, the mean difference in weight loss at 12 months was 7.2 kg (95% confidence interval [CI]: 4.9 to 9.4) with similar effects observed in subgroups defined by age, sex, or baseline BMI. This weight reduction corresponds to a mean difference in BMI of 2.3 kg/m<sup>2</sup> in men and 2.7 kg/m<sup>2</sup> in women. Rates of mild adverse events, defined as those not interfering with normal functioning (constipation, fatigue headache, and dizziness), were higher among those

allocated TDR, while there was no evidence of a difference in rates of adverse events of moderate or greater severity (i.e. events that interfered with normal functioning) between treatment groups.

### **The PRIMETIME-CE Obesity model**

We estimate the accrual of life-years, quality-adjusted life-years (QALYs), and health care costs (in UK 2017 prices) for the UK population by sex and age (in 5-year bands) up to age 100 years using an adapted version of the PRIMETIME-CE model [16, 17]. PRIMETIME-CE Obesity is a population-based proportional multi-state lifetable model that links body mass index (BMI) to mortality and non-communicable disease morbidity (type-2 diabetes, coronary heart disease [CHD], stroke, and cancers of the breast, colon, liver, kidney, and pancreas). A fuller description of the model and all data inputs are detailed in the Supplementary Appendix. An R package has been developed to allow easy use of the PRIMETIME-CE Obesity model, and is available from <https://github.com/seamuskent/PRIMETIME-CE-Obesity>.

The PRIMETIME model consists of a lifetable, which estimates life-expectancy, and disease lifestables, which estimate the incidence and prevalence of, and mortality from, each modelled condition. Disease and mortality rates depend on age, sex, and BMI. The effects of weight loss are propagated through the model by affecting general mortality and the incidence of each condition. Population impact fractions (PIFs) are calculated for each condition and for mortality using the relative risk shift method [18]. PIFs provide an estimate of the proportion by which mortality or disease incidence in the population would be reduced given a change to the BMI distribution, based on the mean weight loss in the target population, the distribution of BMI, and the association between mortality or disease incidence and BMI. They are calculated in each year of the model by sex and age group.

EQ-5D utilities are calculated for each study year based on the age and sex of participants, and the incidence and prevalence of the modelled conditions [19], and combined with life-years to estimate quality-adjusted life-years (QALYs). Mean annual NHS costs per prevalent case of each modelled condition, calculated from NHS Programme Budgeting Returns 2013-14 [20], were used to cost prevalent disease rates in the PRIMETIME model. Intervention costs were evaluated externally to the model. All costs were converted to UK 2016-17 prices using the hospital and community services inflation index [21].

### **Intervention costs**

The cost-effectiveness of the TDR programme is estimated in comparison to a nurse-led behavioural support programme. The nurse-led support programme is estimated to cost £34.06 per-person in year 1, based on an additional 2 minutes of GP time in which patients are referred to the nurse-led support programme (£8.24), and 4 attendances with a nurse practitioner over 12 weeks, each lasting 10 minutes (£25.82). The TDR programme is estimated to cost £796.06 per-person. This is based on an additional 4 minutes of GP time in which patients are referred to the programme and their eligibility ascertained (£16.49), scheduled medication reviews with GPs on two occasions (at baseline and 4 weeks) for the 30% of patients taking medication for diabetes or hypertension (£22.69). Finally, based on observed attendances with the counsellor (mean 12.3 attendances, comprising 315 meal replacement products; see Supplementary Table 1 for further details), we estimated the cost of the TDR part of the programme to be £756.88. This was based on the standard costs of the programme when provided direct to the public with an average cost per product of £2.40 (which is priced to incorporate the cost of the behavioural support).

### **Weight loss beyond 12 months**



In the DROPLET trial, participants were followed for 12 months. There is uncertainty about the trajectory of weight in both trial arms beyond 12 months. We model, therefore, two main scenarios (**Figure 1**). First, we assume that in both treatment arms weight returns to its baseline level in an approximately linear fashion between 12 months and 5 years following the start of intervention. This is in line with evidence that, on average, individuals tend to regain weight following weight loss [22, 23], and the observed reduction in mean difference in weight loss between 6 and 12 months in DROPLET [14]. Second, following the long-term weight change observed in the Diabetes Prevention Program Outcomes Study [5], we assume that 1 kg weight loss relative to baseline weight is maintained beyond 5 years among participants allocated TDR, with weight reaching this level from 12 months in an approximately linear fashion.

### **Base case analysis**

Outcomes are simulated up to 100 years of age for a hypothetical population of adults with obesity, with the same age and sex distribution as of DROPLET study participants, and results are averaged over this hypothetical cohort. We also estimate results within population groups defined by sex, age in fifteen-year bands (20-34, 35-49, 50-64, and 65-79 years), and BMI (30 to <35, 35 to <40, and  $\geq 40$  kg/m<sup>2</sup>), assuming a difference in mean weight loss between TDR and nurse-led behavioural programme in each group of 7.2 kg at 12 months.

We compare the life-years, QALYs, and costs accrued with the two treatment options, and calculate the Incremental Cost-Effectiveness Ratio (ICER), which provides an estimate of the additional costs of TDR for every additional QALY gained. The National Institute for Health and Care Excellence (NICE) typically considers interventions as cost-effective if they have an ICER of less than £20,000 per QALY [24]. For some analyses, we calculate net monetary benefits (NMBs) which are given as the product of the incremental QALYs and the

threshold value (i.e. £20,000 per QALY) minus the incremental costs; a positive NMB indicates that TDR is cost-effective at that threshold.

In the estimation of ICERs and NMBs, future costs and health outcomes are discounted at a rate of 1.5% per annum, based on recommendations by NICE for evaluating preventative programmes in which benefits are expected to accrue over a long time period [25]. When presented separately, life-years and QALYs are not discounted. We perform probabilistic sensitivity analysis using 500 Monte Carlo Simulations to estimate the impact of uncertainty in healthcare costs, quality-of-life decrements, the associations between BMI and disease incidence and mortality, and the effect of TDR on weight loss at 12 months on cost-effectiveness.

### **Scenario and sensitivity analysis**

We undertake a variety of scenario analyses to explore the impact of different modelling assumptions. In particular, we explore the impact of: (1) different combinations of the rate of weight regain and the mean weight loss maintained in the long-term; (2) different total TDR programme costs, including assuming a fixed fee of £907.20 for the TDR programme based on the costs that would be incurred under current retail prices if patients followed the treatment protocol perfectly; (3) discounting health outcomes and costs at 3.5% in line with the NICE guidelines for health technology appraisals [24]; (4) adding further healthcare costs by age and sex [20, 26], for health conditions beyond those included in the economic model; (5) modelling a direct effect on weight loss on EQ-5D utility using the observed difference in EQ-5D per kilogram of weight loss at 12 months in DROPLET of 0.02 [14], in addition to the effect on QALYs operating through disease incidence; and (6) applying the treatment to the general UK population of adults with obesity rather than only to participants with characteristics like those enrolled in the DROPLET trial. We also estimate

the programme cost at which TDR has an ICER equal to £20,000 per QALY, the threshold for cost-effective interventions in UK.

## RESULTS

Compared to the nurse-led behavioural support programme, the TDR programme is projected to generate an additional 0.069 life-years (95% confidence interval [CI]: 0.049-0.089) and 0.065 QALYs (0.047-0.084) at an additional discounted cost of £665 (635-696) per-person over a person's lifetime, or £12,955 (8,082-17,827) per QALY gained, assuming people return to their baseline weight at 5 years following intervention (**Table 1**). The higher total costs for the TDR programme reflect an additional £762 in intervention costs which is only partially offset by £97 (66-127) lower NHS costs related to the modelled diseases. For every 100,000 people referred to TDR, it is projected that 50 (34-66) incident CHD events, 75 (50-100) incident strokes, 899 (658-1140) cases of type-2 diabetes, and 26 (13-38) cancers would be avoided.

If instead it is assumed that participants following TDR maintain a weight 1 kg lower than their pre-intervention weight after 5 years, TDR is projected to be even more cost-effective at £3,203 per QALY gained (95% CI: 2,580-3,825). This reflects higher expected gains in life-years (0.287 life-years; 0.237-0.337) and QALYs (0.245; 0.209-0.281), and a reduced net discounted cost difference of £519 (471-567), as a result of greater projected NHS costs savings.

The incremental cost per QALY is lower for population groups at higher age, independently of sex, under the assumption of a return to pre-intervention weight at 5 years post intervention (**Figure 2**). In this scenario, TDR is cost-effective at a threshold of £20,000 for adults aged 35 years or older, but not for younger adults. For adults aged less than 50 years, the confidence intervals around the mean ICERs include the £20,000 per QALY threshold. Under the assumption of a maintained 1 kg weight loss after 5 years, TDR is cost-effective for all adults. Differences in cost-effectiveness by gender are small. In both

scenarios of future weight trajectory, the incremental cost per QALY is highest in adults with class I obesity (BMI 30 to  $<35 \text{ kg/m}^2$ ) and lowest (i.e., most cost-effective) in adults with class III obesity (BMI  $\geq 40 \text{ kg/m}^2$ ), but consistently below the standard threshold of £20,000 per QALY for all adults irrespective of their BMI at recruitment.

The longer the duration over which costs and health outcomes are projected, the more cost-effectiveness TDR becomes since the costs of treatment are incurred in year 1, while the health benefits and healthcare cost savings are accrued in later years. For the total population, TDR becomes cost-effective at £20,000 per QALY when outcomes are projections over time periods longer than 17 years and 13 years in the scenarios of full weight regain and partial maintenance of weight loss, respectively (**Figure 3**).

The longer weight remains below its pre-intervention level, and the greater the long-term weight loss maintained, the more cost-effective a TDR programme would be (**Figure 4**). Assuming a maintained weight loss of at least 1 kg, TDR is cost-effective at £20,000 regardless of how quickly weight is regained to this level following intervention. In the absence of long-term maintenance of weight loss, TDR is cost-effective at £20,000 per QALY so long as it takes more than 3 years until lost weight is completely regained.

Under the assumption of full weight regain at 5 years, a fixed fee for the TDR programme of £907.20, discounting costs and health outcomes at 3.5% per year, and including additional healthcare costs incurred for diseases beyond those modelled in PRIMETIME increase the ICER from £12,955 to £15,551, £17,673, and £15,300, respectively (**Figure 5**). Including an additional direct effect of weight loss on EQ-5D utility reduces the ICER to £6,039. Applying the model to the entire UK population of adults with obesity rather than trial participants produced very similar results. These alternative scenarios had similar

directional but smaller absolute, impacts on the ICERs when assuming partial maintenance of weight loss, with TDR remaining highly cost-effective at £20,000 per QALY in all scenarios.

The cost-effectiveness of the TDR programme decreases linearly with total programme costs (Figure 6). For the TDR programme not to be considered cost-effective at £20,000 per QALY, it would have to cost £1,157 or more assuming complete weight regain and £3,518 or more assuming 1 kg weight loss is maintained after 5 years.

## DISCUSSION

The DROPLET trial demonstrated that GP referral to a specific TDR programme was a safe and effective treatment for weight loss in adults with obesity [14]. Here we have provided evidence that this TDR programme is also cost-effective under a range of plausible scenarios regarding weight regain after 12 months. It is most cost-effective in middle-aged and older adults, and those at higher levels of BMI, who face higher immediate risks of obesity-related diseases and premature mortality. The cost-effectiveness results were robust to alternative modelling assumptions including in the discount rate applied to costs and health benefits and the inclusion of further healthcare costs for diseases beyond those modelled in PRIMETIME.

This is the first study to estimate the cost-effectiveness of TDR for the routine treatment of obesity. Our estimates were informed by effectiveness data from a recent trial [14], and we were able to extrapolate results based on estimates of associations between BMI and the incidence of obesity-related diseases and mortality from leading epidemiological studies. The PRIMETIME-CE model allowed us to model the effect of weight loss on a range of obesity-related conditions and account for multi-morbidity [27]. We were also able to estimate the impact of small changes in weight, rather than transitions between broad weight categories as in many other models [28], on disease incidence and mortality.

The results presented herein pertain to a specific TDR programme, namely GP referral to a commercially provided low-energy diet programme with behavioural support delivered over six months with gradual food reintroduction after three months. The base-case cost estimate for the TDR programme reflects observed attendance rates among participants in the DROPLET study and current recommended retail prices. In practice it is not clear how this or similar interventions would be organised and financed were the NHS to offer them. There would be some set up costs in procurement of the service but there may also be

opportunities to achieve lower costs of the programme itself through competitive tendering. We estimated that a TDR programme delivering the weight loss observed in the DROPLET study would be cost-effective at £20,000 per QALY as long as the total programme costs were no greater than £1,157, assuming full weight regain at 5 years. However, adherence and, accordingly, effectiveness could also differ under alternative TDR schemes. For example, if the behavioural support was delivered by healthcare practitioners or a co-payment scheme in which patients were expected to contribute to the costs was introduced, adherence to the programme, its price, and hence cost-effectiveness might differ.

There are of course a number of important limitations. First, body weight was only measured for 12 months. We made assumptions about the sustainability of weight loss beyond 12 months based on previous evidence, although most studies were short in duration [22, 23]. In this analysis, we made similar assumptions about weight regain to other studies [8] and the cost-effectiveness of TDR was robust to conservative assumptions about weight regain. Nevertheless, future research would benefit from a better understanding of the durability of weight loss.

Second, we estimated the impact of weight change on disease incidence and mortality from observational studies, which may be subject to bias from residual confounding. Weight loss through surgical or non-surgical interventions is associated with reductions in all-cause mortality and diabetes incidence, and with diabetes remission [4, 5, 29, 30]. Surgical interventions are associated with reductions in the incidence of fatal and non-fatal cardiovascular events [31], and also cancer in women but not in men [32]. Reductions in cardiovascular events and cancer incidence have not been consistently reported in non-surgical interventions [4, 6], but this may relate to low-power and insufficient follow-up in these studies, or the extent to which the dietary intervention affects cardiovascular risk factors [33]. In DROPLET, TDR was shown to improve cardiovascular risk factors at 12 months



[14], and in a similar trial among people with recently-diagnosed type-2 diabetes, 45% of people offered a TDR programme were in remission at 12 months [13]. Future research would benefit from direct randomised evidence on clinical endpoints like disease incidence, remission, and mortality, as well as on healthcare costs and health-related quality of life.

Third, excess weight has been associated with increased incidence and costs of many health conditions not included in PRIMETIME including knee osteoarthritis [2, 34] and weight loss can promote diabetes remission which is not included in the model [13, 35]. Accordingly we may have under-estimated the healthcare savings accruing from weight loss with TDR in obese adults. As is the case with most other analyses, the cost-effectiveness analysis was performed from an NHS healthcare perspective, and did not consider wider societal costs. It did not incorporate any costs to the patient of attendance at the behavioural support sessions but nor did it consider the cost-savings to patients through reduced purchases of their usual food. Finally, we did not model the impact of the higher rates of mild adverse events among those allocated TDR on health-related quality of life or costs. These events, by definition, do not interfere with normal functioning, are confined to the 12 week weight loss phase of the programme, and do not entail large healthcare expenditures. Hence, their inclusion would not be expected to materially impact on cost-effectiveness.

To our knowledge, there are no cost-effectiveness analyses of TDR programmes for the routine treatment of obesity. A number of cost-effectiveness analyses have been undertaken for other surgical, pharmacological, and lifestyle management interventions. Comparability across studies is difficult because of major methodological differences including the comparator(s) chosen, population studied, time horizon, and assumptions about effects of weight loss on quality of life, and weight regain. Bariatric surgery is generally found to be cost-effective with ICERs of £2,000 to £4,000 per QALY gained in patients who are morbidly obese [36]. Although an expensive procedure at around £10,000 [37], it delivers

substantial and sustained weight loss and improved health outcomes [29]. A systematic review of the cost-effectiveness of pharmacological treatments reported a median ICER of £24,000 per QALY for Orlistat [38]. Orlistat reduces weight by about 2.6 kg at 12 months compared to placebo [39], at a cost of around £540 per year [40]. A number of studies have reported on the cost-effectiveness of behavioural interventions for weight loss [8, 9, 41-44]. Most produce modest reductions in weight at 1-2 years, but because they can typically be provided at very low cost, they are often considered cost-effective. For instance, referral to a 52-week community-based weight-loss group offered by a commercial provider produced an additional weight loss of 4 kg at an additional cost of £176.34 compared to brief intervention, giving an ICER of £2,394 per QALY over 25 years [8].

Many previous studies, particularly those of pharmacological interventions, have assumed that weight loss has a direct effect on EQ-5D utility. This is probably a major determinant of the low ICERs reported [38]. Indeed, in our analysis, assuming such an effect substantially reduced the incremental cost per QALY of TDR from £12,955 to £6,039 assuming full weight regain at 5 years. However, a systematic review and meta-analysis of weight loss trials did not find consistent evidence of improvements in health-related quality of life following weight loss [45].

Based on the current retail prices for the diet replacement products, the TDR programme used in the DROPLET trial is a cost-effective treatment for reducing weight in adults with obesity. Low energy total diet replacement programmes are not currently recommended for the routine treatment of obesity [11, 12]. In view of growing clinical and economic evidence, the use of, and funding for, such programmes should be reconsidered.

## **Acknowledgements**

We thank the participants and the staff at the primary care practices who contributed to this study. We also thank Kate Tudor for extracting data on attendances with counsellors, and Peter Scarborough for providing the PRIMETIME-CE model, adapted for this study.

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## TABLES AND FIGURES

**Table 1. Health benefits and healthcare costs over 25-years for nurse-led behavioural support and total diet replacement programme**

	<b>Nurse-led intervention (nurse)</b>	<b>Total diet replacement (TDR)</b>	<b>Mean difference (95% CI) (TDR vs. nurse)</b>
<b>Weight regained by 5 years following intervention</b>			
Life-years	31.31	31.38	0.069 (0.049, 0.089)
QALYs	23.19	23.26	0.065 (0.047, 0.084)
Total costs (£)	7,425	8,090	665 (635, 696)
Treatment costs (£)	34	796	762 (762, 762)
NHS disease costs (£)	7,390	7,294	-97 (-127, -66)
ICER (£ per QALY)			12,955 (8,082, 17,827)
Disease incidence (per 100,000 persons)			
CHD	10,238	10,188	-50 (-66, -34)
Stroke	13,947	13,872	-75 (-100, -50)
Type-2 diabetes	51,142	50,243	-899 (-1,140, -658)
Cancer*	15,005	14,979	-26 (-38, -13)
<b>Maintained weight loss of 1 kg in TDR arm after 5 years</b>			
Life-years	31.31	31.60	0.287 (0.237, 0.337)
QALYs	23.19	23.44	0.245 (0.209, 0.281)
Total costs (£)	7,425	7,944	519 (471, 567)
Treatment costs (£)	34	796	762 (762, 762)
NHS disease costs (£)	7,390	7,148	-243 (-291, -195)
ICER (£ per QALY)			3,203 (2,580, 3,825)
Disease incidence (per 100,000 persons)			
CHD	10,238	10,031	-206 (-256, -157)
Stroke	13,947	13,704	-243 (-356, -130)
Type-2 diabetes	51,142	47,020	-4,122 (-4,651, -3,592)
Cancer*	15,005	14,902	-102 (-146, -59)

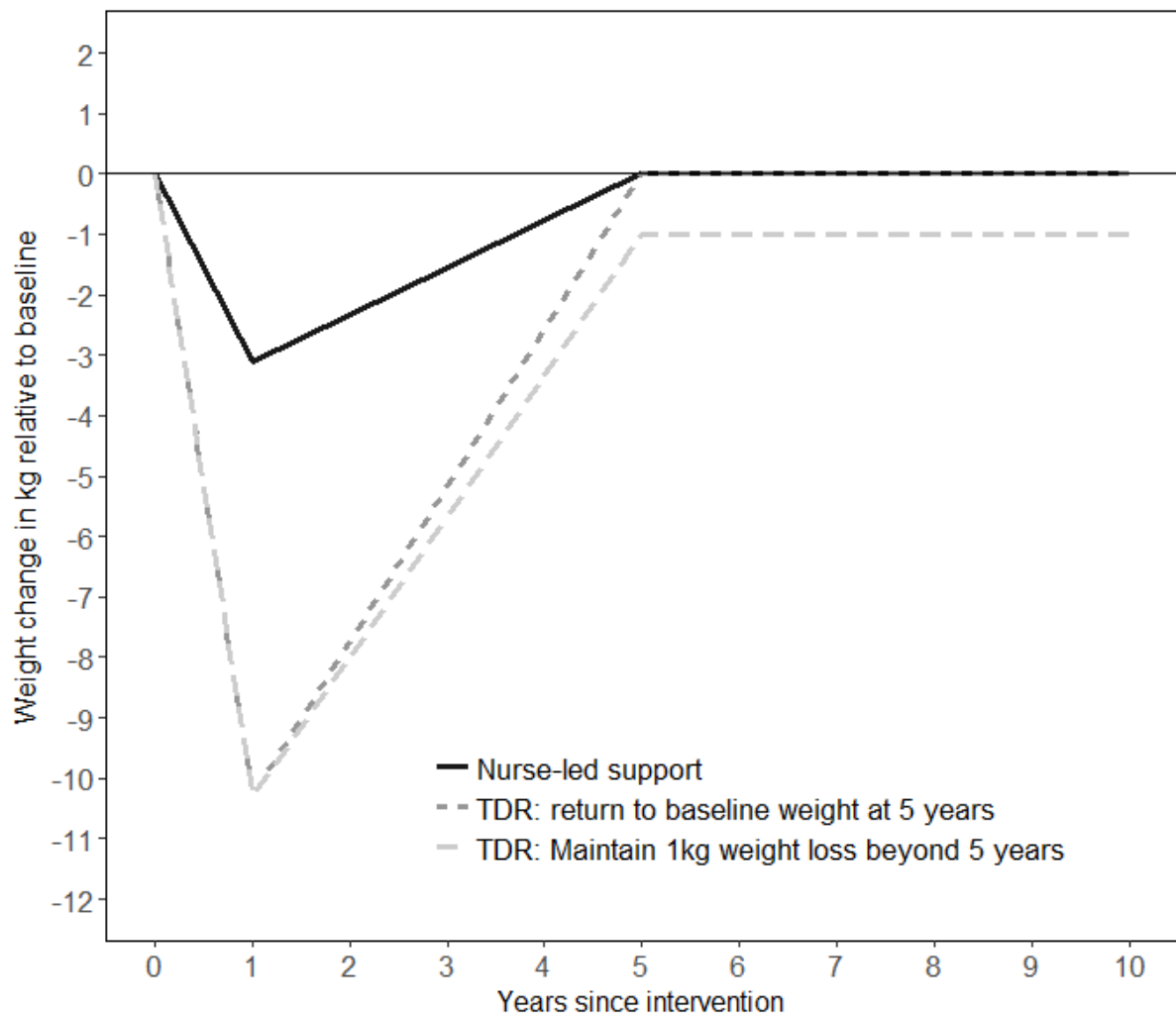
Values are means (95% confidence intervals). All reported values are discounted at 1.5% per annum, except life-years and QALYs which are undiscounted.

QALYs=Quality-adjusted life-year; ICER=Incremental Cost-Effectiveness Ratio;

CHD=Coronary heart disease; NHS=National Health Service; TDR=Total diet replacement.

\*Includes cancers of the breast, colon, liver, kidney, and pancreas.

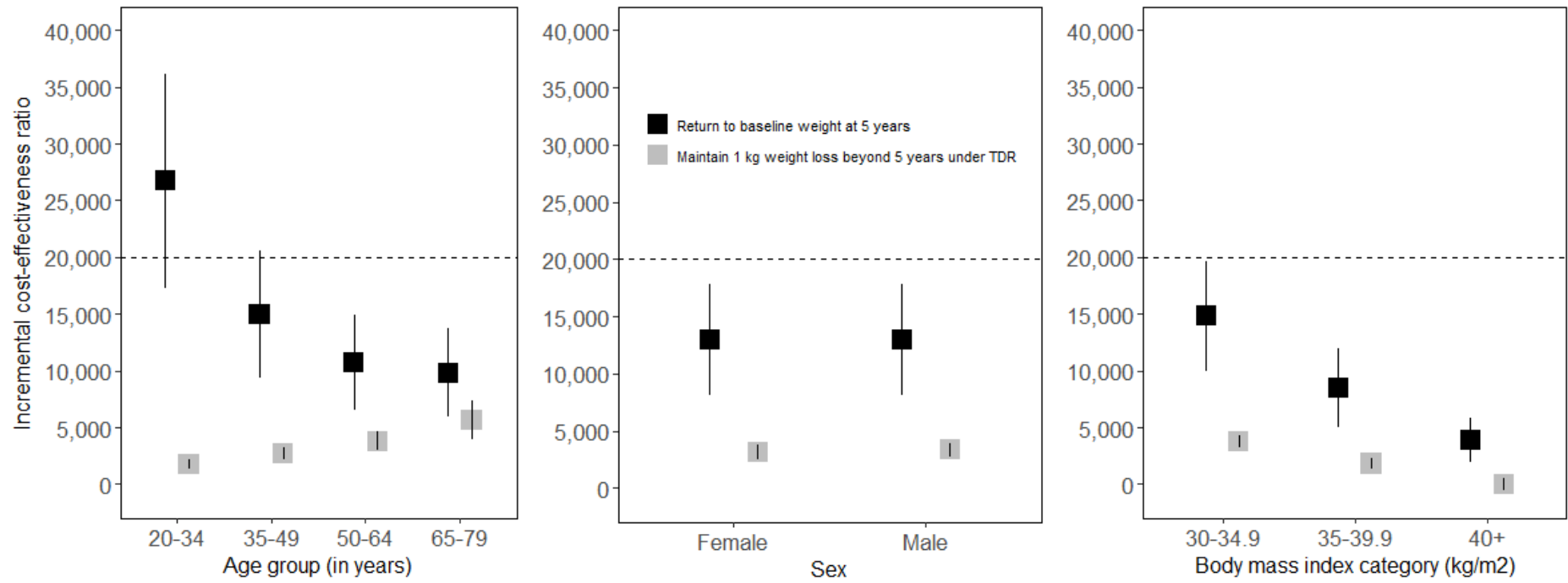
**Figure 1. Weight loss scenarios**



TDR=Total Diet Replacement; kg=kilograms.

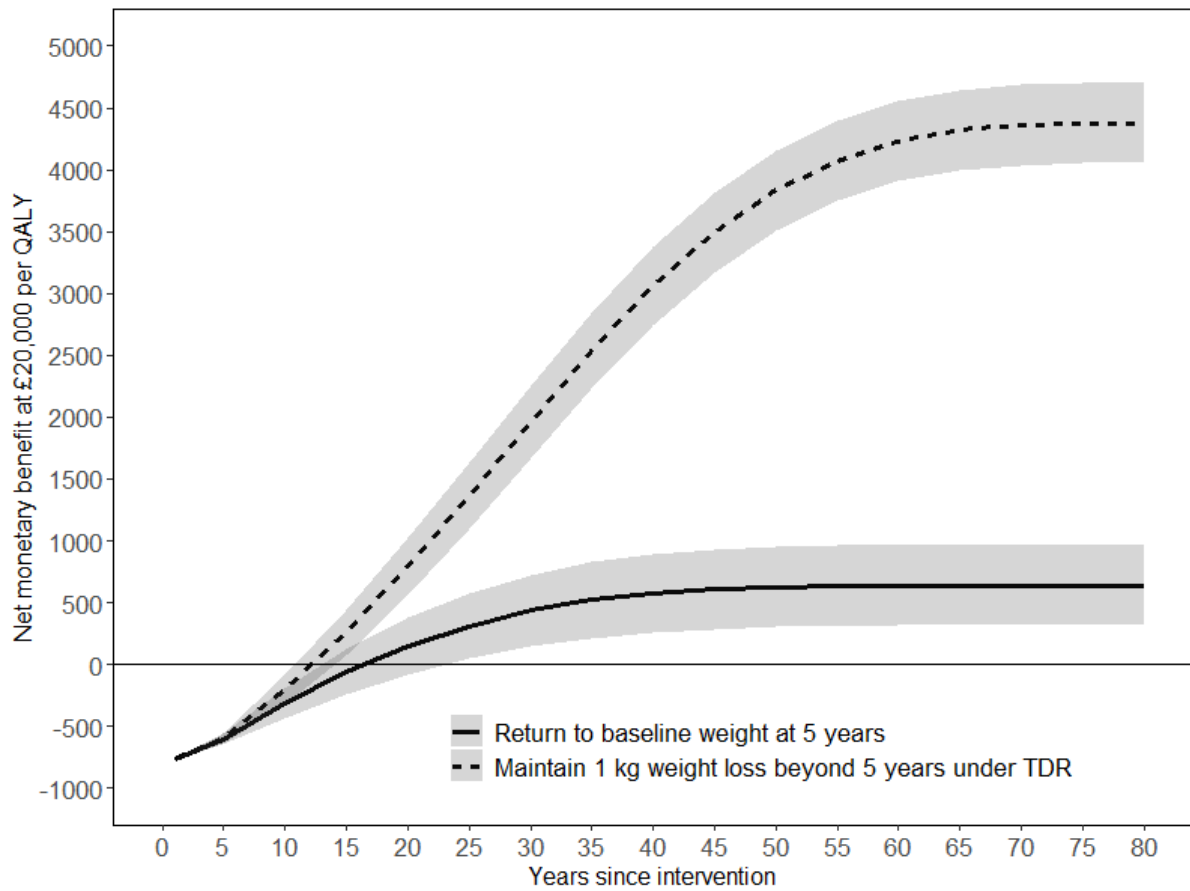


**Figure 2. Incremental cost-effectiveness ratios in subgroups by age, sex, and body mass index**



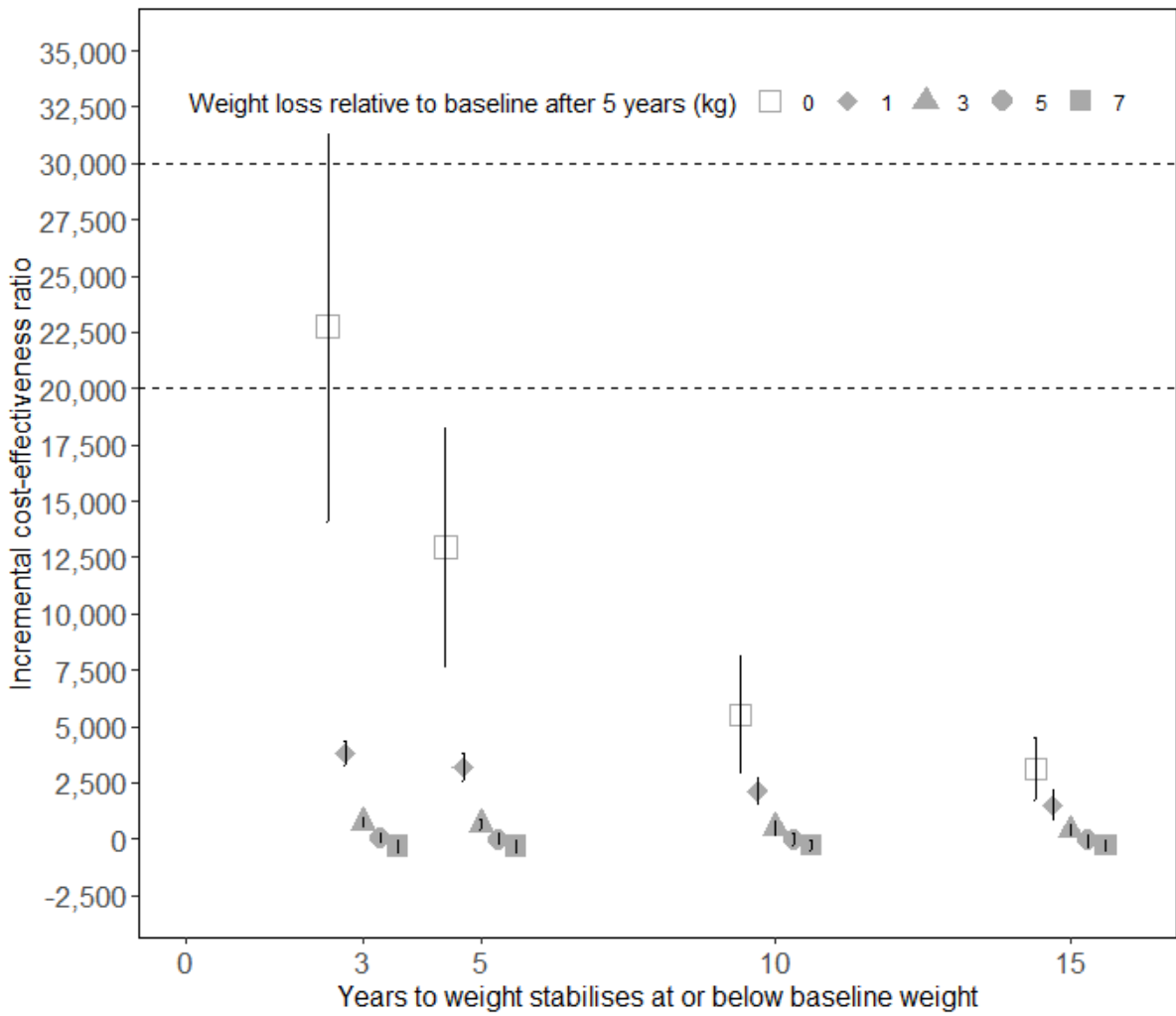
TDR=Total Diet Replacement; kg=kilograms. Error bars show 95% confidence intervals.

**Figure 3. Net monetary benefit over time under different weight trajectory scenarios**



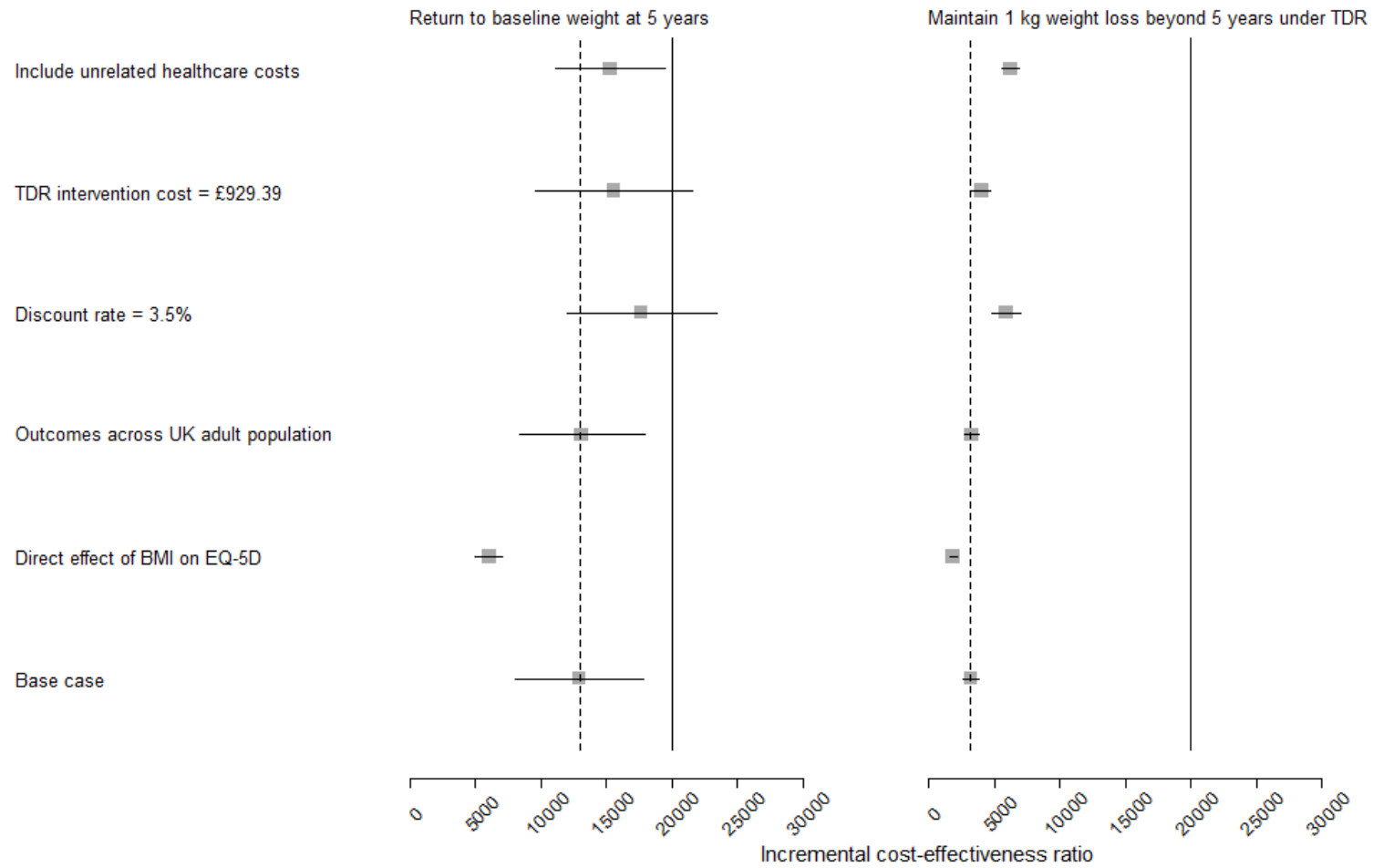
QALY=Quality Adjusted Life Year; TDR=Total Diet Replacement; kg=kilogram. Shaded areas show 95% confidence intervals.

**Figure 4. Incremental cost-effectiveness ratios under different assumptions about future weight trajectories**



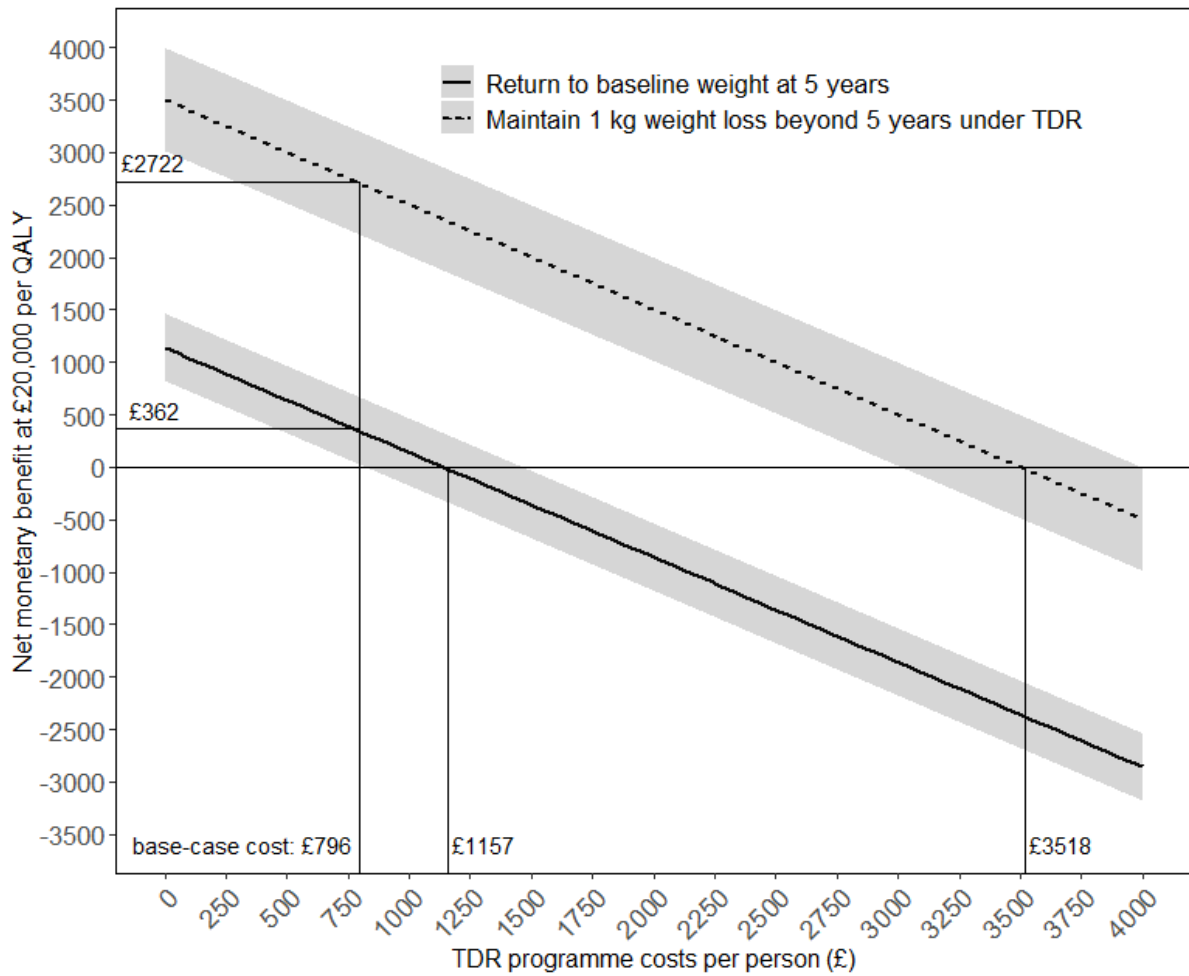
Error bars show 95% confidence intervals.

**Figure 5. Incremental cost-effectiveness ratios under alternative model assumptions**



TDR=Total Diet Replacement; BMI=Body mass index; kg=kilogram. Error bars show 95% confidence intervals.

**Figure 6. Net monetary benefit by total TDR programme costs under different weight trajectory scenarios**



TDR=Total Diet Replacement; kg=kilogram; QALY=Quality Adjusted Life Year. Shaded areas show 95% confidence intervals.