Effectiveness and cost-effectiveness of interventions that cause weight loss and reduce the risk of cardiovascular disease

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Abstract

Background: Overweight/obesity is associated with significant morbidity, mortality and costs. Weight loss has been shown to reverse some of these effects, reducing the risk of chronic diseases such as cardiovascular disease (CVD). We aimed to determine potential monies available, from an English National Health Service perspective, for weight loss interventions to be cost-effective in the prevention of CVD.

Methods: A Markov model was developed, populated with overweight/obese individuals from the Health Survey for England aged 30-74 years, free of pre-existing CVD, and with available risk factor information to calculate CVD risk. All individuals were free of CVD at baseline and with each annual cycle, could transition to other health states of primary CVD, secondary CVD or death according to transition probabilities for a maximum period of ten years, or until death. Utilities, costs and the effects of weight loss on CVD risk factors were applied. The potential monies available for CVD prevention strategies provided the incremental cost-effectiveness ratio met UK arbitrary limits of between £20 000 and £30 000 was determined.

Results: Applying the effects of weight loss on CVD risk factors prevented 12 CVD events and saved 12 quality-adjusted life years over 10 years per 1 000 individuals. £27-£39 was available per person per year for up to 10 years when meeting the UK arbitrary limits.

Conclusions: Individual annual financial allowances for weight loss interventions to be considered cost-effective is relatively low; however, as a

large proportion of the population is affected, wide cheap societal interventions are important.

Introduction

Overweight and obesity, which currently affects approximately 62% of the UK adult population [1], is linked to many chronic diseases such as cardiovascular disease (CVD), diabetes and cancer. The significant morbidity and mortality associated with overweight and obesity imposes a major burden on the healthcare system. The UK Foresight report estimated that in 2007, the annual direct costs to the National Health Service (NHS) of treating overweight and obesity, and related morbidity, was approximately £4.2 billion in England alone [2] and more recently the McKinsey report has estimated the global burden as equivalent to $2 trillion annually [3].

Weight loss, even when modest or unsustained long-term, has been shown to reverse some of the effects of overweight and obesity, and in turn reduce the risk of chronic diseases such as type 2 diabetes [4] and cardiovascular disease (CVD) [5, 6]. Weight-loss interventions include lifestyle interventions (diets to reduce energy intake, increased exercise or physical activity, or their combination) as well as pharmaceutical and bariatric surgical interventions. Just as the extent of weight loss differs between interventions, so too do the costs. For example, bariatric surgery which involves invasive surgery and hospitalization is initially much more expensive than pharmaceutical therapy, which is in turn more expensive than most lifestyle interventions. Whilst cost-effectiveness analyses to investigate the cost-effectiveness of specific interventions in the prevention and treatment of obesity and its related disease have been undertaken, the cost-effectiveness of weight loss (irrespective of the type of intervention used) has not been evaluated as an integrated whole. In this study, we aim to determine the amount of monies available, from an English NHS perspective, for weight loss interventions to be considered cost-effective in the prevention of cardiovascular disease with a particular focus on interventions that result in moderate (5-<10%) weight loss.

Methods

An individual level Markov model was developed in Microsoft Excel to determine the potential monies available for weight loss interventions to be considered cost-effective. In the model, all individuals enter in a healthy state, free of CVD. Individuals then, on a random basis, transition to another cardiovascular health state according to transition probabilities derived from risk prediction algorithms, and population life-tables. Individuals continue to cycle through the model yearly until the time-point of interest is reached. We chose a period of 10 years, in line with current CVD risk prediction algorithms, unless the individual's trajectory leads to earlier death. The possible health states to which an individual could transition can be depicted using a decision-analysis tree (Figure 1). Possible designated resulting states include: alive without cardiovascular disease, alive with cardiovascular disease, dead from cardiovascular disease or dead from other causes. Thus, with each annual cycle, an individual may develop non-fatal cardiovascular disease, or die from cardiovascular disease or other non-cardiovascular causes. All events were considered to occur halfway through an annual cycle.

Transition probabilities

Primary CVD

The annual risk of a primary CVD event was determined using the Framingham risk prediction algorithm [7]. This algorithm uses risk factors of age, sex, systolic blood pressure, total cholesterol, high-density lipoprotein (HDL)-cholesterol, smoking status, diabetes status and the presence or absence of left ventricular hypertrophy (LVH) to determine risk. The impact of obesity is implicitly included in the algorithm. This risk, together with a random number generator, determines which individuals will in fact have an event. For example, if a patient's probability of a primary CVD event in a cycle is 0.176 (17.6%) and the random number generated is 0.163 (16.3%), the patient is assumed to have a primary CVD event. If the random number is 0.53 (53.0%), however, the primary CVD event does not occur. Once an individual is classified as having a primary CVD event, the event is proportioned out into different types of CVD events including unstable angina, stable angina, CHD, CHD death, transient ischaemic attack (TIA), stroke, and stroke death, according to age and sex, as per distributions in the ScHARR model [8]. With each annual cycle, annual changes in modifiable risk factors such as systolic blood pressure, total and HDL-cholesterol, as well as BMI were also applied. These annual changes were calculated using the evidence from the Health Survey for England [1] and Framingham risk was re-calculated.

Secondary CVD

The risks of secondary events were sourced from a Health Technology Assessment report for an economic evaluation of statins for the prevention of coronary events [8], which provided annual transition probabilities by age and sex. These risks were dependent on the type of primary CVD event (e.g. CHD or stroke event), and included secondary non-fatal MI, non-fatal stroke, fatal MI and fatal stroke.

Death from other causes

The risk of dying from other causes was determined using data from the Office for National Statistics 2010 for England and Wales only [9], calculated as the difference between all-cause mortality and circulatory deaths. This was stratified by age and sex.

Population

Individual subject data was gathered from the Health Survey for England [1] in 2011. Only those of adult age 30 to 74 years old in keeping with the Framingham risk prediction algorithm age specifications, free of pre-existing CVD, who were overweight/obese (BMI $\geq$25 kg/m^2), and with all necessary risk factor information available to calculate risk of CVD according to the Framingham risk prediction algorithm were included, with the exception of LVH which is not routinely collected and therefore was assumed to be absent in all individuals. Changes in modifiable risk factor levels were calculated using the Health Survey for England 2008-2011 data, stratified by BMI, sex, and 10-year age bands. From these, annual changes within age-bands were derived assuming linear changes. Since the absolute risk of CVD is low in a young adult population, we also undertook a sub-group analysis in a population 40 years and older. A sub-group analysis stratified by BMI was also undertaken to assess the effects of weight loss in each weight category.

Effect of weight loss

Data on the effect of weight loss on CVD events as such are limited. There is, however, extensive evidence on the impact of interventions that cause weight loss on cardiovascular risk factors. We recently conducted a systematic review and meta-analysis on the effect of interventions that cause weight loss on cardiovascular risk factors at different time points (6-<12 months, 12-<24 months, and ≥24 months) [10]. We excluded bariatric surgery as this causes extreme and rapid weight loss, is only appropriate in severely obese individuals, and only a very small minority are able to access it [11]. In our model, we only included the risk factor effects present in the Framingham risk prediction algorithm (systolic blood pressure, total cholesterol, and HDL-cholesterol). The effects of interventions that cause weight loss on cardiovascular risk factors were stratified by different degrees of percentage weight loss (0-<2.5%, 2.5-<5%, and 5-<10%). Sub-analyses assessed the effect of percentage weight loss on cardiovascular outcomes, assuming 100% compliance. Input data, however, came from our meta-analysis, where the percentage weight loss encapsulated participants that did not have a 100% compliance or success with weight loss interventions. See Table 1 for input values. Interventions which extended beyond 24 months' time point were typically 24-<36 months in duration. For cycles in the model after 36 months (4-10 years), both a best and worst-case scenario was explored. In the first instance the effects of weight loss on cardiovascular risk factors were set to zero i.e. that there were no subsequent effects associated with the weight loss on cardiovascular risk factors (a conservative estimate). In the second analysis, the effects of weight loss on cardiovascular risk factors were assumed to remain the same throughout the 10-year period as those observed at 24 months.

Utilities

All individuals in the model were assigned a quality of life value or utility according to their BMI; which was age- and sex-specific. If they were deemed to have a cardiovascular event, the utility decrement associated with the cardiovascular event was then applied (see Table 2) [8].

Costs

Costs of cardiovascular events were taken from the ScHARR cost-effectiveness model and were based on a thorough review of the most recent and appropriate costing information [8]. They are summarised in Table 2. Costs included direct costs of myocardial infarction, stable and unstable angina, stroke, transient ischaemic attack (TIA), as well as fatal CHD and fatal stroke, measured for the first year of the event and after the first year. All costs were inflated from 2004/2005 values to reflect 2015 costs according to the UK national health price index [12]. All future benefits (QALYs) and costs were discounted at 3.5% per annum.

Outcomes

The outcomes of interest we studied were the number of QALYs prevented and the potential monies available for prevention strategies provided the incremental cost effectiveness ratios (ICERs) met arbitrary limits set out in terms of UK pounds per year per QALY saved. We calculated ICERs by comparing the difference in net costs between treatment (weight loss) and no treatment (control), divided by the difference in QALYs lived by each cohort. The arbitrary threshold for ICERs is between £20 000 and £30 000 [13]. We employed both threshold limits to determine the potential monies available for prevention strategies over 10 years.

Results

1 544 individuals from the Health Survey for England 2011 met the criteria for inclusion in the model. The average age of these individuals was 53 years (standard deviation (SD) 12.1), 52.4% of whom were female. The average BMI was 30.1 kg/m^2 (SD 4.4). Cardiovascular risk factors were slightly elevated [systolic blood pressure: 128.9 mmHg (SD 16.0); HbA1c: 5.8% (SD 0.8); total cholesterol: 5.5 mmol/L (SD 1.1)], with the exception of HDL-cholesterol, which was above the accepted mean normal value (1.1 mmol/L) measuring 1.4 mmol/L (SD: 0.4). 12.0% of the population were smokers and 6.3% had diabetes.

When the effects of weight loss (see Table 1) on CV risks were applied to the individuals included in this model, 12 cardiovascular events were prevented, 12 QALYs were potentially saved over 10 years per 1 000 individuals when the effects after 36 months were set to nil, and 20 cardiovascular events were prevented and 42 QALYs saved when the effects after 36 months were set to that seen at $\geq$24 months, compared to placebo. Based upon a cost-effectiveness threshold of £20 000/QALY, the potential monies available to provide a weight loss intervention would be £27.42 and £91.63 per person per year for up to ten years respectively. At a £30 000/QALY threshold, the cost of cost-effective interventions would be £39.02 and £133.94 respectively.

When weight loss was stratified by percentage weight loss (0-<2.5%, 2.5-<5%, 5-<10%), the number of cardiovascular events prevented, the number of QALYs saved and the potential monies available increased with increasing weight loss (Table 3). In line with the results seen in the main analysis, when the treatment effects after 36 months were set to maintain 24-<36 months outcomes, the number of CVD events prevented, number of QALYs saved and potential monies available were greater than when they were set to the conservative scenario of no sustained weight loss effects.

Applying the effects of weight loss on CV risks to an older population of adults aged 40 to 74 years, prevented more cardiovascular events than when the whole population was included (Table 3).

Applying the effects of weight loss to only those who were only overweight prevented slightly more events than when both overweight and obese were included, but with lower annual permitted expenditures (Table 4). The reverse was seen when the effects of weight loss were applied to only those who were in the obese category.

Discussion

Weight loss has been shown to reduce cardiovascular risk factors, events and improve quality adjusted life years [10]. In England the provision of short-term, non-clinical weight management (so-called Tier 2 services) are commissioned at a cost of between <£50 to £400 (most frequently reported £100/participant) [14]. Tier 3 services represent more complex interventions, clinically led, targeted at those with severe and/or complex obesity, but are very scanty. Where they exist, the cost is reported to be >£400/patient [14]. We have explored what sums of money could be spent on weight loss interventions that would meet NICE criteria for cost-efficacy [15].

Interventions that cause weight loss could potentially gain between 10 and 26 QALYs for a population of 1 000 individuals aged 30 to 74 years who were overweight/obese and free of existing CVD, over 10 years. According to the arbitrary thresholds of affordability equal to £20 000 to £30 000 per QALY gained, between £27 and £134 could potentially be spent per person each year for up to ten years on weight loss interventions. When weight loss was stratified by percentage weight loss (0-<2.5%, 2.5-<5%, 5-<10%), greater reductions in weight resulted in more QALYs gained and therefore the potential for greater financial inputs for prevention strategies. As expected, when the effects after 36 months were constant and remained the same as at 24-<36 months, the results were more pronounced than when the effects after 36 months were set to null. However, this was not apparent when the effects of 5-<10% weight loss were considered. This finding may simply reflect the absence of data obtained in the systematic review for the long term effects of sustained 5-<10% weight loss rather than something specific to this greater weight loss achievement. Furthermore this scenario is likely to be overly conservative since there is clear evidence from a number of lifestyle intervention programs that benefits of diabetes prevention persist in the long-term [16].

Unsurprisingly, analysis of the older age group (age 40 to 74 years), demonstrated that a greater number of cardiovascular events could be prevented when the benefits after 24 months were maintained, compared to the whole population of 30 to 74 year olds. The number of QALYs saved, were also greater. Since CV events in younger age groups are fewer than in older adults, this finding may change if whole lifetime benefits (rather than a 10 year follow-up) were to be modelled. Furthermore if adults ≥75 years were included, then their far higher absolute risk could potentially have enhanced the benefits over a subsequent decade of weight loss and reduced cardiovascular risk. However the Framingham risk prediction algorithm excluded those older than 74 years.

Our model has demonstrated that the potential monies available for weight loss strategies in the prevention of CVD can range from £27 to £134 per person per year for ten years, dependent on the population, amount of weight loss, long-term effects of weight loss, and cost-effectiveness threshold employed. Whilst many intervention strategies have been reported as far dearer than this [17, 18], this amount is within current spending on Tier 2 services in England.

Our findings therefore support 'investment' in making access to treatment programmes more readily available, even if they produce 'only' modest weight losses of about 5%, and even if this weight is not sustained long-term. This may include relatively cheap community wide wellness programs such as free or subsidised exercise classes [19]. As the risk of overweight and obesity escalates with age there will be greater justification for applying rather more expensive interventions for this older portion of the population.

Several analyses have been made of the benefits and cost-efficacy of pharmaceutical interventions [20, 21]. Benefits are wider than just those on the cardiovascular effects analyzed in this modelling exercise. Interestingly the application of 'stopping rules' (i.e. discontinuing medication) in non or poorly responding patients is now widely included in the regulatory approval process and can enhance safety, efficacy and cost-efficacy. Regulatory measures which aim to change the nature of societal eating patterns by imposing checks and taxes on advertising of inappropriate foods and drinks, taxing sugary drinks and fast foods are all capable not only of raising government revenue but, if they allow even modest weight loss on a population basis, important costs savings for the health services. Purely on a cardiovascular basis the benefits are likely to be great provided the costs of implementation through regulatory measures are small for governments. If these and additional measures which reduce hypertension and population lipid levels (e.g. by continuing to reduce salt [22] and saturated fat intakes) are implemented, the benefits in reducing cardiovascular disease will be amplified.

A number of features of our study limit its robustness. First, although the Framingham algorithms are widely accepted, they do not always predict cardiovascular events in other populations accurately. Furthermore these algorithms generated from a general population in practice underestimate cardiovascular risk in some higher-risk populations, such as those with diabetes. It is also clear that without long-term data on the overall impact of weight loss interventions on cardiovascular events it is unclear whether the benefits are cumulative, progressively increase, or decrease. Therefore in our analyses we performed an assessment of the impact of interventions that cause weight loss on cardiovascular risk over an extended duration, on both a best and worst-case basis. When we assumed conservatively that there were no further benefits after 36 months of weight loss, this worst case scenario limited the scale of the benefit. However, a recent study [23] found that any weight loss, even if not sustained, was associated with decreases in carotid intimal thickness and improvements in the cardiovascular risk-factor profile, suggesting that weight loss, at any age in adulthood, is worthwhile and could result in long-term cardiovascular benefit. This so-called 'memory effect' of weight loss has been well demonstrated in a number of diabetes prevention programmes [24, 25, 26, 27] and suggests that interventions that are not sustained may still have profound and long-lasting value.

A further limitation of our model pertains to our model population who may not be representative of the general UK population. Whilst our population was sourced from a national health survey, our rates of smoking were lower than observed in the larger Health Survey for England dataset, the General Lifestyle

Survey and the Smoking Tookit Study [28]; this may reflect some selection bias as individuals with any missing variable data were excluded. Our population, therefore may be 'healthier' than the general population. Employing a 'lower' risk population in our model could result in an underestimation of the true cost effective benefits of weight loss interventions in the UK.

Finally, the effects of weight loss on other outcomes was also not included. Weight loss has been shown to be beneficial for other outcomes such as cancer, osteoarthritis and depression [29, 30, 31, 32]. The reduction in disease would not only decrease costs associated with treatment, but also improve the quality of life for the individual. The omission of other weight loss outcomes in our model further adds to the conservative estimate of the true effectiveness and cost-effectiveness of weight loss interventions in the UK.

Conclusions

The findings from this study demonstrate circumstances under which interventions that cause weight loss may be cost-effective in the prevention of CVD. The individual annual financial allowance for selective cardiovascular preventive measures from weight loss alone is small to gain savings in health care costs, but still higher than is being spent by public health and clinical commissioning groups at present. However, with such a large proportion of the population overweight or obese and with cardiovascular disease still the major cause of death and disability, the need for population wide cheap societal interventions to limit weight gain and encourage weight loss are particularly important and could substantially reduce the health services costs.

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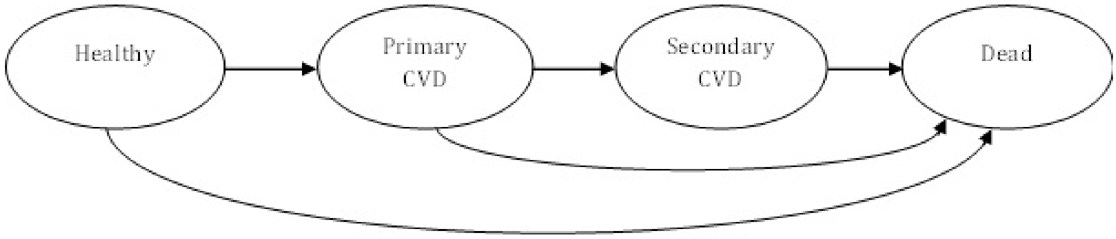

Figure 1: Potential progressive health states during the 10 years of the model.

Table 1 Input parameters including the changes in cardiovascular risk factors associated with interventions that cause a) any weight loss, b) 0-<2.5% weight loss, c) 2.5-<5% weight loss, d) 5-<10% weight loss and e) any weight loss restricted to those aged ≥40 years

a)

	Year		
	1	2	3
SBP (mmHg)	-2.675	-1.570	-1.549
TC (mmol/L)	-0.247	-0.092	-0.076
HDL-C (mmol/L)	0.003	0.005	0.039
BMI (kg/m^2)	-0.776	-1.247	-0.752

b)

	Year		
	1	2	3
SBP (mmHg)	-2.102	-1.395	-2.236
TC (mmol/L)	-0.103	-0.154	-0.096

HDL-C (mmol/L)	0.007	0.007	0.020
BMI (kg/m^2)	-0.448	-0.456	-0.352

c)

	Year		
	1	2	3
SBP (mmHg)	-3.025	-1.707	-0.666
TC (mmol/L)	-0.582	0.039	-0.034
HDL-C (mmol/L)	0.010	0.007	0.050
BMI (kg/m^2)	-0.881	-1.001	-0.969

d)

	Year		
	1	2	3
SBP (mmHg)	-4.861	-1.417	-0.790
TC (mmol/L)	-0.672	-0.431	
HDL-C (mmol/L)	-0.079	0.013	0.044
BMI (kg/m^2)	-1.579	-2.209	

e)

	Year		
	1	2	3
SBP (mmHg)	-2.439	-1.570	-1.582
TC (mmol/L)	-0.268	-0.092	-0.077

HDL-C (mmol/L)	0.006	0.005	0.030
BMI (kg/m^2)	-0.751	-1.247	-0.472

SBP: systolic blood pressure; TC: total cholesterol; HDL-C : high-density lipoprotein cholesterol; BMI: body mass index; and changes in BMI associated with weight loss were only included for annual changes in risk factors and determination of utility purposes.

Table 2: The cost at the time of the event and in subsequent years of having had different types of cardiovascular events, and the respective annual QALY decrement subsequent to the year of having an event.

Input variable	Costs (£)		QALY decrement	Source
	Year 1	Subsequent years		
MI	5 615	216	-0.072	8
Stable angina	216	216	-0.126	8
Unstable angina	555	216	-0.126	8
Stroke	10 156	2 730	-0.185	8
TIA	1 343	333	-0.088	8
Fatal MI	1 472			8
Fatal stroke	8 888			8

MI: myocardial infarction; TIA: transient ischaemic attack; all costs were 2015 costs (inflated from 2004/05 costs as per the UK National Price Index).

Table 3: Differences in the number of primary and secondary events and the quality-adjusted life years (QALYs) gained from different degrees of weight loss for 1 000 individuals over ten years. The potential monies available for prevention of cardiovascular disease (CVD) to ensure cost savings for interventions that cause weight loss and its effect on cardiovascular risk factors

is set out assuming either only short term benefits for the first 36 months of weight loss (nil effects) or continuing benefits for the whole 10 year period (same effects).

	Number of Primary CVD events	Number of Secondary CVD events	QALYs gained	Annual permitted expenditure at two different Cost-effectiveness thresholds	
				£20 000	£30 000
30-74 year population with any weight loss					
Nil effects	7	5	12	27.42	39.02
Same effects	13	7	42	91.63	133.94
Percentage weight loss					
0-<2.5%					
Nil effects	7	5	4	11.83	15.64
Same effects	13	7	21	48.88	69.82
2.5-<5%					
Nil effects	8	5	14	32.57	46.38
Same effects	14	8	52	111.85	164.04
5-<10%					
Nil effects	9	5	26	56.30	81.94

Same effects	12	7	29	63.96	92.68
40 -74 year population with any weight loss					
Nil effects	8	6	14	33.54	47.88
Same effects	15	9	47	102.48	149.58

Where any weight loss represents any weight loss (0->10% change in body weight); nil effects represents zero effect of weight loss on cardiovascular risk factors after 3 years; same effects represents same effects of weight loss on cardiovascular risk factors after 3 years as at year 3.

Table 4: Differences in the number of primary and secondary events and the quality-adjusted life years (QALYs) gained for 1 000 overweight/obese individuals over ten years, stratified by starting BMI. The potential monies available for prevention of cardiovascular disease (CVD) to ensure cost savings for interventions that cause weight loss and its effect on cardiovascular risk factors is set out assuming either only short term benefits for the first 36 months of weight loss (nil effects) or continuing benefits for the whole 10 year period (same effects).

	Number of Primary CVD events	Number of Secondary CVD events	QALYs gained	Annual permitted expenditure at two different Cost-effectiveness thresholds

				£20 000	£30 000
BMI					
25-<30 kg/m^2					
Nil effects	9	4	0	3.81	3.58
Same effects	15	6	28	63.52	91.76
30-<40 kg/m^2					
Nil effects	4	0	20	42.03	61.54
Same effects	9	4	56	116.46	172.01

Where nil effects represent a zero effect of weight loss on cardiovascular risk factors after 3 years; same effects represent the same effects of weight loss on cardiovascular risk factors after 3 years as at year 3.