The University of Sheffield
ScHARR School of Health and Related Research
NICE Public Health Collaborating Centre

Prevention of type 2 diabetes: preventing pre-diabetes among adults in high-risk groups

Report on Use of Evidence from Effectiveness Reviews and Cost-effectiveness Modelling

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About the ScHARR Public Health Collaborating Centre

The School of Health and Related Research (ScHARR), in the Faculty of Medicine, Dentistry and Health, University of Sheffield, is a multidisciplinary research-led academic department with established strengths in health technology assessment, health services research, public health, medical statistics, information science, health economics, operational research and mathematical modelling, and qualitative research methods. It has close links with the NHS locally and nationally and an extensive programme of undergraduate and postgraduate teaching, with Masters courses in public health, health services research, health economics and decision modelling.

ScHARR is one of the two Public Health Collaborating Centres for the Centre for Public Health Excellence (CPHE) in the National Institute for Health and Clinical Excellence (NICE) established in May 2008. The Public Health Collaborating Centres work closely with colleagues in the Centre for Public Health Excellence to produce evidence reviews, economic appraisals, systematic reviews and other evidence based products to support the development of guidance by the public health advisory committees of NICE (the Public Health Interventions Advisory Committee (PHIAC) and Programme Development Groups).

Contribution of Authors

The modelling team comprised Mike Gillett, Alan Brennan and Laurence Blake. Maxine Johnson and Emma Everson-Hock provided further analysis of the evidence from Reviews 1 and 2. Helen Buckley Woods undertook the economic literature searches. Monica Hernandez advised on use of the Health Survey for England dataset. Nick Payne and Jim Chilcott were the senior leads. Elizabeth Goyder was the topic expert.

Acknowledgements

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LIST OF ABBREVIATIONS

BME	Black and Minority Ethnic groups
BMI	Body Mass Index
CHD	Coronary Heart Disease
CI	Confidence Interval
CVD	Cardiovascular Disease
HDL	High-density lipoprotein
HSE	Health Survey for England
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
HRQoL	Health-related Quality-of-Life
PACE	Patient-centered Assessment and Counseling for Exercise and Nutrition
SBP	Systolic Blood Pressure
SES	Socio-economic status
TC	Total Cholesterol
UKPDS	United Kingdom Prospective Diabetes Study

EXECUTIVE SUMMARY

This report describes in detail the methods for producing scenarios for actual interventions and “what-if scenarios”, and the methods used to develop the economic model. In summary, the model and the cohort of patients that have been analysed have the following features:

- a representative sample of the England and Wales population using over 15000 individuals from the most recent Health Survey for England
- individual Health Survey for England (HSE) records have information on key risk factors for diabetes and cardiovascular disease including BMI, age, sex, blood pressure, cholesterols, smoking, ethnic group, social class/socio-economic group as well some information on behaviours including quantity and frequency of exercise and portions of fruit and vegetable intake
- the scope of the economic model will be similar to a model for treatment of obesity given that several risk factors are impacted by these interventions including BMI, blood pressure and lipids
- baseline risk of incidence of diabetes is estimated using QDScore, a risk function which includes BME status and an indication of socio-economic status using the Townsend score
- the benefit of reducing BMI on risk of diabetes will be based on intervention studies
- risk of incidence of CVD is estimated using QRISK®2, a risk function which includes BME status and an indication of socio-economic status using the Townsend score
- both QDSCORE® and QRISK®2 have the advantage of being based on large and recent UK datasets with recent validation of QRISK®2 published in BMJ
- from an initial list of 14 potential intervention scenarios, 5 were found to be suitable for inclusion in the modelling, considering quality of evidence and whether they are a genuine community intervention
- each of the 5 interventions is assessed in the low SES group from where the evidence comes; the what-if scenarios are assessed in several target population groups, e.g. the whole population, low SES groups, high BME populations and a combined low SES and high BME populations
- initial effects of the intervention on risk factors e.g. effects on BMI, SBP and Total:HDL are assumed to have reversed by year 4
- the long-term risk factor progression after the initial 1 year effect of the intervention including the natural history of progression of the risk factors is modelled

- In each year estimating the risk of CVD and risk of developing diabetes, and simulating the incidence of these outcomes, with separate analyses for individuals receiving the intervention and individuals receiving 'usual care'
- applying a cost of care to incident and prevalent cases of CVD and diabetes
- applying loss of health utility score to incident and prevalent cases of CVD and diabetes in order to calculate quality adjusted life years (QALYs)
- counting up the discounted costs and discounted QALYs in both the intervention and 'usual care' arms and computing the incremental cost-effectiveness ratio for the scenario intervention / subgroup modelled.

The results show that the cost-effectiveness is, in most of our analyses, most strongly determined by the Initial Intervention cost, the ongoing Support Costs, the intervention effect size, whether the Intervention is targeted at the whole population or obese only, and the durability of beneficial effects. To a lesser extent, it is determined by whether the intervention is targeted at the BME and low SES subgroups (versus the overall population)

Two of the intervention scenarios (dietary/nutritional advice promoting increased fruit and vegetable intake, and opening of a new food retail outlet) did not demonstrate cost-effectiveness – this is because the estimated effects on markers of CVD risk and diabetes are not significant enough to result in a reduction in events.

The modelling suggests that Interventions 3 (broad dietary education/cooking skills), 6 (Multi-component – small scale intervention), and 9 (Large-scale, region-wide multi-component (like Hartslag Limburg) are cost-effective based on the mean reported effects. Intervention 9 appears to be not only highly cost-effective but also possibly cost-saving (depending on assumptions around cost of maintenance intervention).

The results also highlight the need to achieve sustainable benefits (reduction in BMI etc) beyond just the first year in order for interventions to be cost-effective. As intensive individual-based NHS resources comparable to those available to intensive diabetes prevention trials are likely to be prohibitive (both from a cost and resource availability point of view), designing affordable but effective maintenance interventions beyond the first year will need to be a key consideration.

1. BACKGROUND

1.1. Purpose of this report

Evidence from systematic reviews of the effectiveness of community-based interventions in low socio-economic status (SES) and Black and Minority Ethnic (BME) groups has been presented in Reviews 1 and 2 respectively. For the modelling, we are particularly interested in studies that report the biomedical measures that are included in the QRISK®2 and QDScore® equations that will be used for estimating risk of CVD and Type 2 diabetes respectively, i.e. BMI, systolic blood pressure and total:HDl cholesterol ratio. Where studies have not measured such biomedical measures, it is often still possible to estimate these from reported changes in behavioural outcomes, e.g. increase in fruit and vegetable intake, or increase in exercise. In such cases, we have used HSE cross sectional data to estimate via statistical regression the effects of changes in behavioural measures on BMI, SBP, and the Total:HDL cholesterol ratio.

11 potentially useable studies were found in four broad categories – advice on diet and nutrition, physical-activity-related interventions, retail interventions, and composites of all three. Given the paucity of results from large studies in Reviews 1 and 2, we have also identified and examined evidence from some wider international sources and non BME/SES populations. Altogether, this has led to the specification of 14 intervention scenarios.

The above evidence will be used as a basis for economic modelling to answer questions concerning the effectiveness and cost-effectiveness of alternative community-based interventions in different defined sub-populations at risk of pre-diabetes.

1.2. The role of economic evaluation within the NICE process

The original purpose of NICE was to advise the National Health Service (NHS) on the effectiveness and cost-effectiveness of clinical-management strategies and health technologies. Since 2005, this remit has expanded to the wider public sector with respect to public health. The NHS, and more generally the public sector, has limited resources yet demands are essentially unlimited. Where money is spent on a new intervention, existing interventions will be displaced. Therefore, a rational and coherent framework is required to help to inform decisions about which interventions are considered to be economically attractive to society.

Within a cost-effectiveness analysis, the additional costs and benefits of a new intervention are compared with those of the current standard intervention over a sufficient period to capture these differences. It is important to capture all consequences of an intervention, and hence it is appropriate for many health economic models to compare costs and outcomes over a lifetime. A new intervention can be considered cost-effective if it generates more benefits to patients than it displaces as a result of any additional costs imposed on the system. An economic model is required to objectively combine data from a number of different sources and to make projections into the future. Inevitably within models, assumptions are required which simplify reality. For example, assumptions are required to be able to estimate future costs and benefits using current data. There will always be some uncertainty associated with the model structure and the model parameters and, therefore, around the model results as a consequence of the assumptions required to develop the model. The strength of the available evidence and the uncertainties around the relationship between costs and outcomes in the present and costs and outcomes in the future will impact upon the model results.

In order to assess the impact of the key assumptions within the model upon the model results, a sensitivity analysis is required. A sensitivity analysis involves varying model assumptions to assess the impact of a different assumption to that made within the base case (the main results presented) upon the model results. If varying an assumption in some sensible way has a large impact upon the model results, then more information may be required around that parameter or structural assumption in order for the model to be able to inform the decision. However, if varying a parameter or assumption has a limited impact upon the model results, then the model results can be considered to be reasonably robust to that assumption. If all of the key assumptions are tested within a sensitivity analysis and they all have a limited impact upon the model results, then there is more certainty that the model results are illustrative of the truth. The benefits of a new intervention can be measured in terms of disease-specific/ topic specific outcomes. A diagram of the calculation of cost-effectiveness of an example intervention such as a group weight management programme (WMP) compared with no such provision is shown in Figure 1 below.

The resulting Incremental Cost Effectiveness Ratio (ICER) may be presented in terms of a Cost-Effectiveness Plane as shown in Figure 2 below. Within this figure the cost and effectiveness of current standard practice is denoted by the origin. The additional benefits and costs generated as a result of each of the interventions assessed are then plotted on the x- and y-axis respectively.

Figure 1 : Example of economic evaluation of Weight Management Programme (WMP)

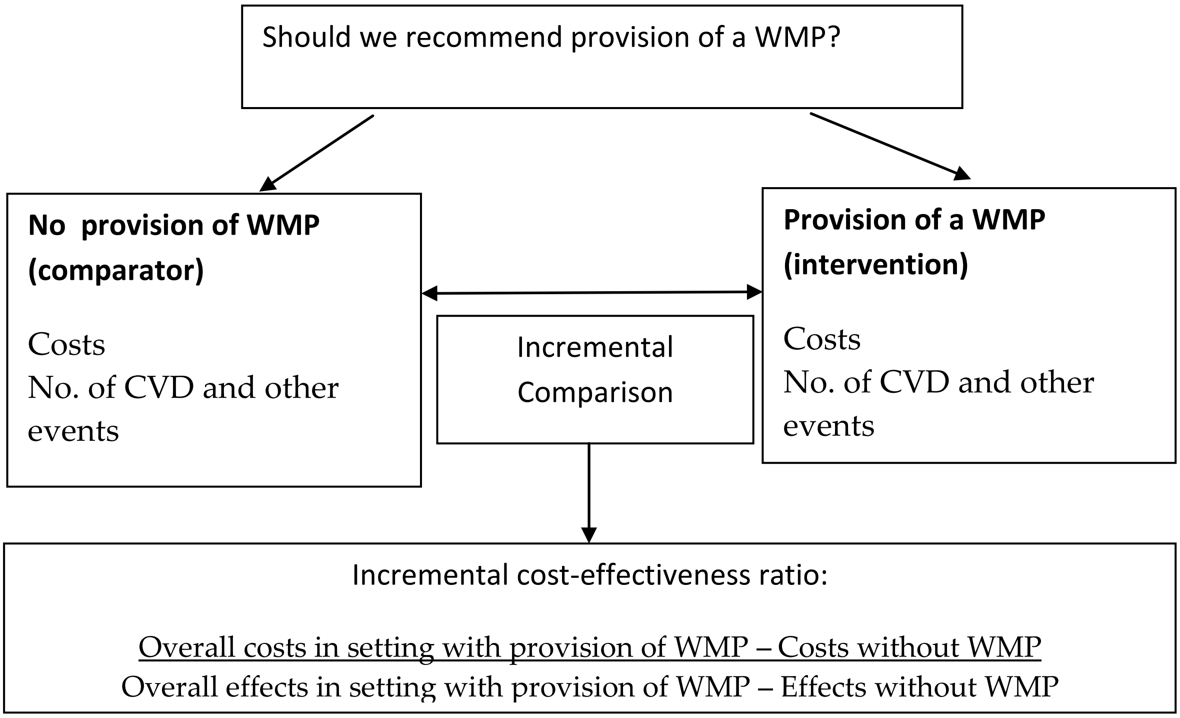
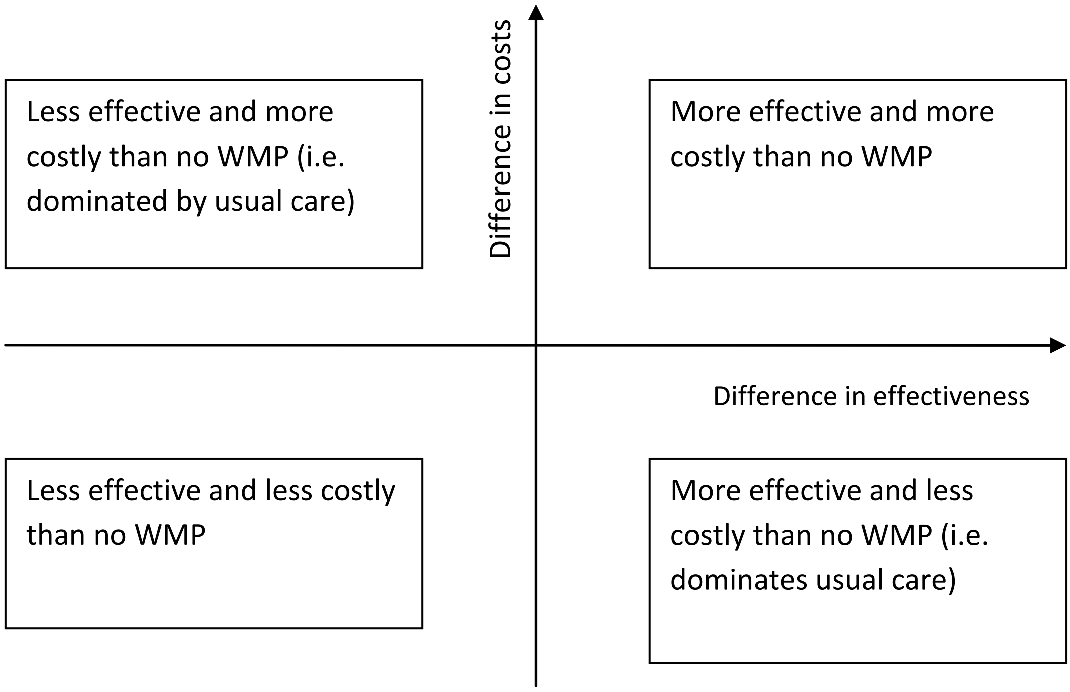


Figure 2 : Cost-effectiveness plane for Weight Management Programme (WMP)



Interventions which fall into the north-west quadrant of the plane would not be considered as cost-effective in comparison to current standard practice. Conversely, interventions which fall into the south-east quadrant of the plane would be considered to be economically attractive in comparison to current standard practice as they are estimated to be more effective and cost saving in comparison to current standard practice. The cost-effectiveness of interventions which fall into the north-east or south-west quadrant of the plane are less clear as they are more effective and more costly or less effective and less costly than current standard practice respectively. In these cases, the decision maker must decide how much they are willing to pay for a measure of effect. In order to be able to compare the cost-effectiveness of interventions over different disease areas and populations, NICE usually uses the cost per quality-adjusted life year (QALY) gained of the new intervention compared with current standard practice. In order to calculate the cost per QALY, a health utility score (where 0 is a notional health state equivalent to being dead and 1 is a notional health state equivalent to full health) is estimated for each of the states within the economic model. The total utility scores of each person are weighted over the time frame of the model according to time in each state to produce the total QALYs gained for the new intervention compared with the current standard practice. NICE suggest that the opportunity cost of other interventions displaced by the new intervention is around £20,000 - £30,000 per QALY gained per person. Interventions which are more effective than the comparator and are estimated to have a cost per QALY gained of less than £20,000 - £30,000 are therefore considered to be economically attractive, and hence appropriate for introduction and adoption in England and Wales (NICE, 2009).

Within the current analysis, only outcomes specific to the disease area are calculated. As prevention of prediabetes is likely to involve some form of lifestyle behaviour change, similar to interventions for obesity, relevant outcomes are primarily cardiovascular events, diabetes, osteoarthritis and obesity-related cancers. Any potential impacts of changed survival rates on incidence of non-obesity-related disease as a result of the intervention are not included.

The cost-effectiveness ratio may differ according to the perspective from which costs and effects are incurred. The reference perspective for NICE public health is the public sector perspective. This involves considering all costs incurred by the public sector.

2. METHODS

2.1. Evidence for effectiveness of interventions from UK studies in BME groups and low socioeconomic groups

Two systematic reviews, effectiveness reviews 1 and 2, have been undertaken by ScHARR. Briefly, these reviews have examined interventions in low socioeconomic groups and BME groups respectively. This section summarises suitable evidence from these for the modelling.

The core risk factor driving the estimation of future obesity-related events is BMI, this variable being the common variable included in risk equations for CVD, diabetes and osteoarthritis. A few relatively small studies report BMI (or weight) but most just report behavioural outcomes. Lifestyle interventions often result in changes to other cardiovascular risk factors such as systolic blood pressure (SBP), total cholesterol and high-density lipoprotein (HDL) cholesterol so these were also extracted where reported.

11 studies were found in total reporting change in BMI, weight or behavioural factors.

2.1.1. Studies reporting change in BMI

The three studies are summarised in Table 1 below. Unfortunately, there was only one study (Williams) in BME groups but this was excluded because there was no control arm and the study only included 13 patients. Although the study by Gray 2009 also had no controls, with a 4-year duration, outcomes were deemed to be more reliable as any placebo effects would be more likely to wear off by the 4-year point. This study had 110 patients.

Table 1 : BMI and other biomedical data for intervention (I) versus control (C)

Study	Intervention type & details	Duration	Sample size	BMI baseline	BMI Follow-up	SBP baseline	SBP Follow-up	TC baseline	TC Follow-up	HDL-c Baseline	HDL-c Follow-up
McKellar 1	Dietary/ nutritional - Mediterranean-type diet	6 mths	130	I : 25.86 C: 27.65	I : 25.39 C: 28.22	I : 132 C: 130	I : 128 C: 130	I : 5.55 C: 5.3	I : 5.3 C: 5.4	I : 1.55 C: 1.6	I : 1.5 C: 1.6
Steptoe	Dietary/ nutritional - Behavioural counselling	12 mths	271	I: -0.01 C: 0.04 Adj. diff 0.04 (95% CI -0.25 to +0.33)		I : -0.80 C: -0.56 Adj. diff -0.24 (95% CI -3.50 to +3.02)		I : -0.09 C: -0.07 Adj. diff -0.02 (95% CI -0.17-0.12)		-	-
Gray	Multi-component (NHS Weightwatchers -style intervention)	Up to 49 mths	110	I : -1.29 change from baseline		-	-	-	-	-	-

TC = Total Cholesterol

In Gray, blood pressure was not reported so it is unknown whether the large BMI reduction was accompanied by a reduction in blood pressure

[1] Reported change in total : HDL ratio in control arm is not consistent with the separate changes in total cholesterol and HDL

2.1.2. Studies reporting behavioural data (where BMI not reported)

Where studies only reported behavioural data, an assessment was made (as detailed in section 2.1.4) as to whether changes in other reported outcomes (e. g. portions of fruit and vegetables) could be mapped to changes in BMI.

Table 2 : Dietary/nutritional studies

Study	Intervention type & details	Duration	Sample size	Portions per day baseline	Portions per day Follow-up
Studies focussing on fruit and vegetable intake					
Ashfield-Watt	Dietary/nutritional – Improving awareness, attitudes & access to fruit & veg	1 year	1554	I : 4.8 C: 5.6	I : 4.6 C: 5.1
Bremner 2006	Dietary/nutritional - 5 a day community health promotion	1-2 years	98640	I : 3.36 C: 3.49	I : 3.64 C: 3.64
Studies focussing on overall diet					
Wrieden 2006	Informal educational sessions	6 months	93	I : 1.2 C: 1.3 Change from baseline : I: 0.09 C: 0.04	I : 1.3 C: 1.4

Table 3 : Food retail studies

Study	Intervention type & details	Duration	Sample size	Portions per day baseline	Portions per day Follow-up
Cummins 2005	Opening of a new large retail outlet	12 mths	603	I: 3.92 C: 4.16	I: 4.91 C: 4.6
Wrigley 2003	Opening of a new large retail outlet	12 mths	1009	tbc	tbc

Table 4 : Multicomponent intervention studies

Study	Intervention type & details	Duration	Sample size	No. days exercise per 4 weeks - baseline	No. days exercise per 4 weeks - Follow-up
Lindsay 2008	Access to an internet portal, 'Hearts of Salford'	6 mths	108	I: 14.52 C: 14.2	I: 15 C: 15.56

Comments :

The following studies were excluded, either on the basis that there was no means of mapping reported outcomes to BMI, or because of lack of a control arm and/or small sample size:

Dobson 2000 (small sample size, no control)
Kennedy 1998 (‘percentage of patients with decreased fatty food intake’ could not be mapped to BMI change)
Kennedy 1999 (no measures that could be mapped to BMI change)
Cochrane 2008 (‘percentage of patients more active’ could not be mapped to BMI change)
Baxter 1997 (‘percentage of patients exercising’ could not be mapped to BMI change)
Lowther (fitness assessment arm only omitted – considered too intensive to be of practical use)

2.1.3. Synthesis of evidence on behavioural outcomes

Despite a dearth of evidence for the effect of interventions on BMI and weight, it is possible to create realistic scenarios based on behavioural outcomes. Firstly, a synthesis of the behavioural evidence was undertaken for each type of intervention (e.g. fruit and vegetables).

2.1.4. Mapping behavioural outcomes to biomedical measures

Some of the studies did not record specific outcome data necessary for the calculation of QRISK® (see Section 2.9.1.1) and QDScore® (see Section 2.9.2), but reported only changes in diet or the level of exercise. To estimate the potential magnitude of these intervention effects on some of the more important risk factors, the relationship between the behavioural outcomes and biomedical measures (BMI, systolic blood pressure, total cholesterol and HDL cholesterol) was explored using the cross-sectional Health Survey for England data and linear regression analysis. The comparison of people whose current lifestyle incorporated elements of the desired intervention outcomes to various degrees, gave a measure of the likely benefits obtainable. Table 5 shows the regression results with the effect of frequency of exercise and level of fruit and vegetable intake on BMI, systolic blood pressure and total:HDL cholesterol ratio. Fruit and vegetable intake was recorded as the total number of portions consumed in the previous week, while exercise was the number of days over the previous four weeks that an individual had taken over thirty minutes of exercise. The regressions controlled for the main other factors that influence these measures, that is, age, gender and social class..

Multivariate regression analyses were undertaken to determine the independent effects of exercise and fruit and vegetable intake on BMI, SBP and lipids

Table 5: Results of Regression analyses

Table 5a: analyses with 'physical activity' covariate defined as occasions per 4-week period doing at least 30 minutes of exercise

Outcome	BMI			Blood pressure			Log(Total : HDL cholesterol ratio) *		
	Coeff.	Std. Error	Sig.	Coeff.	Std. Error	Sig.	Coeff.	Std. Error	Sig.
Constant	24.825	0.259	0.000	114.869	0.974	0.000	1.459	0.200	0.000
Age	0.050	0.003	0.000	0.405	0.010	0.000	0.002	0.000	0.000
Gender	-0.460	0.092	0.000	-5.896	0.343	0.000	-0.175	0.007	0.000
Social class	0.280	0.035	0.000	0.522	0.129	0.000	0.015	0.003	0.000
Fruit and veg.	0.028	0.019	0.127	-0.113	0.070	0.105	-0.004	0.001	0.024
Exercise	-0.019	0.004	0.000	0.005	0.016	0.739	-.001	0.000	0.000

* natural log

The regression shows that people who eat more fruit and vegetables on average have a significantly lower cholesterol: HDL ratio, while for those who have an active lifestyle the benefits extend to a lower BMI.

Table 5b: analyses with 'physical activity' covariate defined as average hours doing all physical activities for 30+ minutes per week - including occupational activity

Outcome	BMI			Blood pressure			Log (Total : HDL cholesterol ratio) *		
	Coeff.	Std. Error	Sig.	Coeff.	Std. Error	Sig.	Coeff.	Std. Error	Sig.
Constant	24.543	.232	.000	114.762	.869	.000	1.433	.018	.000
Age	.053	.003	.000	.406	.009	.000	.003	.000	.000
Gender	-.466	.092	.000	-5.862	.342	.000	-.175	.007	.000
Social class	.297	.035	.000	.506	.129	.000	.016	.003	.000
Fruit and veg.	.029	.019	.118	-.119	.070	.087	-.004	.001	.007
Exercise	-.026	.005	.000	.024	.018	.182	-.001	.000	.000

* natural log

The synthesised behavioural outcomes were then mapped to biomedical measures for each intervention type (e.g. fruit and vegetables).

This approach to linking behaviours to risk of diabetes and CVD, rather than applying evidence for the direct effect of behaviours on risk, has been taken because the latter would not be robust without the availability of hazard ratios adjusted for covariates included in the QRISK®2 and QDScore® algorithms.

2.1.5. Costs of interventions

The reported or estimated costs of the above interventions are summarised below –

Study	Cost per patient	Cost reported (R) or estimated (E)	Resource use details
McKellar	£ 84	R	6-week cookery course, composed of weekly 2-hour sessions • ≤10 participants in each session (similar to DESMOND) • Delivered by nutritionists and teaching staff from local colleges, with advice from occupational therapy staff on the provision of aids for food preparation Folder given to each participant containing information on a Mediterranean-type diet, healthy eating and recipes
Steptoe	£ 59	E	Delivered as two 15-minute individual consultations, two weeks apart (assumed to be by a specialist nurse)
Gray	£ 180	E	12-week weight management programme with four main components: 1. A 40min appointment at a men's health clinic 2. A pre-programme assessment: 20min individual appointments 3. The weight management programme: Each group (max 12 men) met over 3 months, in 12 1-hour evening sessions ... Modelled on an initiative from NHS Forth Valley dietitians 4. Post-programme meetings: Held quarterly at Camelon (for 4 years?)
Ashfield-Watt	£ 42	E	These initiatives involved building community networks to achieve and sustain increased fruit and vegetable intakes through collaboration between

			retailers, educators, primary care teams, employers and local media (in five deprived areas) Assumed to be delivered by a community health promotion worker
Bremner	tbc	E	Activities include home delivery services, improving transport to local markets, voucher schemes, media campaigns, growing and cookery skills, and promoting networking among existing healthy food groups Detail on delivery personnel or duration of the programme was not reported; however it may be assumed that the programme lasted for at least one year (between the pre- and post-programme surveys) Assumed to be delivered by 1.5 WTE health promotion staff
Wrieden 2006	£ 62	E	Two to three hour group session for 10 weeks. Informal educational session covering food hygiene, nutrition and food tasting and a standardised two hour food skills intervention programme delivered over seven weeks. Delivered by CookWell project worker/facilitator (assumed to be health promotion professional)
Cummins 2005	Cannot be estimated		Provision of a new food hypermarket within the intervention area.
Wrigley 2003	Cannot be estimated		The opening of a new large-scale food retail outlet, opened in November 2000. Was on the site of a previous local shopping complex, which had become run-down with many shops closed.
Lindsay 2008	tbc		intervention group received new computers and a one-year broadband subscription along with training and access to the project's portal, Hearts of Salford, which contained discussion forums. Drop-in sessions were available as was phone-in support for any technical difficulties; however, the intervention group was better informed about drop-in sessions as these were promoted by the portal

There is potential for some overestimation of costs where estimated if drop-out rates in studies were significant and some costs are variable rather than fixed (i.e. incurred on an individual patient basis).

2.1.6. Discussion of evidence base in BME groups and low socioeconomic groups

Given the weak data found in Reviews 1 and 2 and lack of economic evaluations, the PDG agreed to draw on existing NICE guidance on interventions that address risk factors for developing pre-diabetes within the general population[2].

In addition, other economic literature was identified through prior experience in this field, advice from PDG members, and 'berry-picking' methods that include citation searching, related articles identified through search tools such as Pubmed and Google Scholar.

2.1.7. International literature & non-BME/SES literature

High-profile non-UK economic studies were considered to be a potential useful source of effectiveness data. Also, although patients with pre-diabetes and diabetes were excluded from the scope, a few studies in these populations have been referred to because components of lifestyle interventions are similar regardless of the prevalence of pre-diabetes in the target group and because either they relate specifically to low SES or BME groups, or they are considered to be a good example of a pragmatic adaptation of proven lifestyle interventions tested in RCTs. Numerous studies were found, varying from small-scale local pilots aiming to replicate the large diabetes prevention studies to large-scale programmes. As a result it is critical to know what the unit cost (per participant) of the intervention is. As costs are not always reported, we have therefore broken down this literature according to whether cost information is available (or can be estimated from details of resource use) as shown in Table 6.

Table 6 : Studies reporting cost of the intervention

Intervention type (Authors); Country/setting	Details : No. of patients (intvn / control); Duration of intervention; Duration of follow-up	Proportion in high-risk groups	Outcome Measure	Results	Resource use/ cost per patient	Comments
Workplace individual counselling (Holland)	N = 131 /168 9 months (7 consultations); 9 months	Few (study was office-based civil servants)	BMI SBP Total Chol	-0.22 (-0.47 to +0.03) No significant effect -0.18 (-0.36 to -0.01)	€ 430	Counselling was based on the individual's stage of behavioural change using PACE physical activity and nutrition protocols
Jacobs-van der Bruggen[1] (modelling study)	N = 2414 / 758 5 years; 5 years[2]	-	BMI Physical activity	Minimum effect -0.05 Maximum effect -0.25 Minimum effect – no change Maximum effect-15% of inactive individuals increase their level of physical activity (to moderately active).	€4.50 per Inhabitant; €6 per adult >20 years of age	Effectiveness scenarios based on review of published community-based studies; intervention costs based on Hartslag Limburg
DEPLOY Pilot Study[3] (Greater Indianapolis, USA)	N = 77 in total and the entire core curriculum was delivered over 16–20 weeks; 4-6 months & 12–14 months	82% white. Average age 58 and comorbidity score of 3 (on scale of 0 to 23)	4–6 months % change in weight % change BMI Total chol 12–14 months % change in weight % change BMI Total chol	 -4.0% -3.5% -0.7 -4.2% (abs diff 4.1kg) -5.3% -0.7	$205 for the 16 sessions[4]; and $325 annually [2]	16 classroom-style meetings focused on building knowledge and skills for goal setting, self-monitoring, and problem-solving. Program sessions lasted 60–90 minutes

[2] This contrasts with $1476 for the first year of the original DPP intervention

OECD economics of obesity review (Table 2)	Worksite intervention	-	Change in BMI	-0.5	$ 77.13	Large employers (would cover estimated 5.8% of population)
	Mass media campaign		Fruit / vegetables (g/day) Physical activity (% of active)	+18.4 + 2.4%	$ 2.27	
	Fiscal measures		Fruit / vegetables (g/day)	+8.6	$ 0.28	Fiscal measures have wider economic effects than purely those captured by health-related QALY changes so this was be deemed to be an unsuitable scenario for modelling
	Food advertising regulation		BMI	- 0.12 to – 0.18	$ 7.11	Would target 20% of the population
	Food advertising self-regulation		BMI	- 0.06 to – 0.9	$ 0.51	Would target 20% of the population
	Food labelling		BMI	- 0.02	$ 3.18	Would target 70% of the population

Table 7 : Studies reporting resource use data allowing us to estimate the cost of the intervention

Study; Country	**Details : No. of patients (intvn, control); Duration of intervention; Duration of follow-up**	**No. of patients; Proportion in high-risk groups**	**Outcome Measure(s)**	**Results : effect of intervention, change from baseline (95% CI)**	**Resource use/ Estimate of cost per patient**	**Comments**
Hartslag Limburg[5]; region-wide strategy aimed at all inhabitants in Maastricht Region (specifically at low	N = 2414 in study (though whole 185,000 regional population targeted), 758 people selected as control from a	Approx 50% in low SES Low SES subgroup	BMI SBP (mm Hg) Total Chol HDL BMI SBP (mm Hg)	~ - 0.3 ~ -6.7 ~ 0.0 ~ -0.0 -0.27 - 6.1	€ 4[6]	This involved a hugely varied mix of 590 major programs. Some interventions were very cheap (e.g. lifestyle seminars, the 'nutrition party' and cycle tours), whereas others involved very high costs, such as the interventions called 'Exercise TV', 'Tasty and Healthy' and 'Focus on Heart and Sports'.

socioeconomic status groups; Holland	'reference region' 5 years; 5 years		Total Chol HDL	0.04 0.02		60% of the investment was on improving exercise.
Television-delivered observation of videotaped weight loss sessions (Meyers[2]); USA	n = 77 (all groups) Duration not reported 15 months	Not reported	Weight (kg)	-3 (versus controls)	£ 15 (rough estimate of cost of DVD)	
Mayer-Davis et al[7] - weight management strategies for black and white adults with diabetes who live in a medically underserved community; USA	12 months; 12 months	medically underserved rural communities	Weight loss (kg)	3 kg at 6 months, 2.2 kg at 12 months	£ 350	16 weekly core sessions, biweekly follow-up for 2 months, and monthly follow-up for the remaining 6 months Regular use of group setting (3 group classes to 1 individual class)
Parikh[8]; USA. a Pilot Diabetes Prevention Intervention in East Harlem, New York City: Project HEED; USA	178 in total	Participants were predominantly Spanish-speaking, low-income, undereducated women	Weight	-2.2kg	Not available	Intervention was a peer-led lifestyle intervention group

Table 8 : Studies not reporting sufficient resource use data to estimate the cost of the intervention

Study; Country	**Details : No. of patients (intvn, control); Duration of intervention;**	**Proportion in high-risk groups**	**Outcome Measure**	**Results**	**Resource use**	**Comments**

	Duration of follow-up					
Mathews et al 2007 (Khush Dil - a cardiovascular risk control project for South Asians UK	n =140; Goal-setting at baseline visit; Follow-up at 6 -12 months	100% South Asians	BMI SBP Total Chol	-0.30 (-0.49 to -0.12) - 3.7 (-6.7 to -0.98) -0.19 (-0.37 to -0.10)		Single arm study; Multi-faceted intervention
UKADS Study; UK – a nurse-led culturally sensitive enhanced care package in UK general practice to improve CVD risk factors in South Asian patients with type 2 diabetes	n = 868, 618 2 years; 2 years	Patients with established diabetes (weight loss may be harder)	Weight/BMI SBP Total chol HbA1c	"No difference" −0·33 (−2·41 to 1·75) - 0·03 (−0·04 to 0·11) −0·15 (−0·33 to 0·03)	Economic analysis suggests that the intervention was not cost effective (incremental cost-effectiveness ratio £28 933 per QALY gained)	Not very intensive which perhaps explains lack of notable benefits (intervention included link workers, who were trained to undertake advocacy and offer culturally appropriate advice for patients during and between consultations with their health-care professionals. Additional educational support for health-care professionals was offered by community-based nurses specialising in diabetes. suggested lack of education and tailoring to cultural needs may be reasons for poor results{2602}.
Whittemore; a real-world adaptation of the Diabetes Prevention Programme in the US)	N= 31, 27 6 months	45% white, 92% female, obese, moderately-low income adults at risk of T2DM	5% weight loss	25% of lifestyle participants achieved a 5% weight loss goal compared to 11% of participants in standard care		These results were obtained with a lifestyle program of much shorter duration than the DPP (4 hours vs. 12-16 hours)

Abbreviations/Units : BMI – kg/m^{2}Total chol - mmol/l, HDL - mmol/l, SBP = systolic blood pressure – mmHg, HbA1c - %

The study by Proper and co-workers 2004 on workplace counselling, that was included as a Public Health intervention in the modelling for the NICE Obesity Guidance, was judged to be non-relevant because it was individual rather than community-based.

Notes to the evidence above –

- from the NICE Prevention of obesity guidance, we only used data from studies that the PDG selected at the time, with consideration to the relevance to the UK with the necessary available evidence. The family-based intervention by Israel et al 1985 as reported in the review by McLean[9]) was excluded as it related to adolescents.
- The studies by Proper and co-workers were included within the public health interventions section of the NICE Obesity Guideline Economics Chapter but may not be classed as community interventions for the purposes of this project.
- The effectiveness for the initial weight loss for the interventions in the obesity guideline modelling appears to be scenario-based given lack of adequate RCT data. The base case assumed intervention led to the achievement of weight maintenance for 1 year (as opposed to the underlying natural history increase of 1kg p.a.) for the 75% of patients that respond. Patients were assumed to return to their baseline weight after one year.
- Chapter 16 of the NICE obesity guideline covered 'clinical interventions' – apart from the Meyers 1996 study, these appear to involve 1-to-1 or very small group sessions (e. g. 6 people) so are not considered community interventions. These typically cost at least £100 per patient and often several times that figure.
- We observed that in the Finnish Diabetes Prevention study, a 4.2kg weight loss was associated with a 4mmHg reduction in SBP. A similar proportional association was reported in a systematic review of lifestyle interventions[10], although this may be limited to follow-up periods of 2 to 3 years, possibly reflecting the fact that regardless of maintained weight loss, blood pressure often reverts back to higher levels.

2.1.7.1. Discussion of international literature

An economic analysis by Bemelmans[6] referred to a review by Kahn which concluded that community-based approaches may decrease average bodyweight by 0.6% and a BMI decrease of approximately 0.2 kg/m2 for an average person. Bemelmans noted however that results varied from a reduction of 0.7kg in some to others reporting no effect – this is not surprising given the variation in intensity of interventions.

Of note, in the low SES subgroup of the Hartslag study, results were only marginally less favourable than the overall group. Also, Lowther noted that socially and economically deprived communities were not hard to reach and responded well to physical activity interventions.

Where studies achieved a weight loss of the order of 2-3 kg (or BMI reduction of around 0.8kg/m^2), these have involved much more intensive 1-to-1 interventions such as the Dutch SLIM project in which the estimated cost per patient was €871 for attendees of the fitness program and €434 for non-attendees[6].

There are a number of single-arm 'Before and After studies', the usefulness of which is debatable. Over a long duration, placebo effects are more likely to disappear revealing the true intervention effect, although there may be other confounding drivers of change (e.g. national-level incentives to improve care such as QOF targets in the UK). A review of 7 community-based attempts to translate the DPP reported various studies but most of these appeared to be single arm and/or small studies[11]. Also, the single arm, well-known GOAL program in Finland reported a 3-year average weight-loss of around 1kg[12]. Similarly, there was an average 0.5 BMI reduction. These averages nevertheless appear to mask a large variation between individuals, as indicated by the standard deviations. The GOAL program consisted of six sessions of task-oriented socio-behavioural group counselling by public health nurses over a period of 8 months. The protocol included no other formal post-intervention contact with the participants, except follow-up measurements at years 1 and 3 but the improvements were sustained from year 1 to year 3. More impressively, the single arm Montana Diabetes Control Program, which involved an average of 14.5 one-hour sessions over 6 months in a group size ranging from 8 to 34 participants, resulted in a mean weight loss of 6.7kg (range –18.0 kg to +2.8 kg) and BMI reduction of 2.4[13].

Self-selection of patients (i.e. the most motivated) and selective attrition can causes overestimates of treatment effects in studies of weight loss[14].

2.2. Intervention scenarios

2.2.1. Evidence-based scenarios

Set out in Table 10 below are the intervention scenarios based on studies initially identified, with pooled estimates of effectiveness (weighted by study sample size).

Based on discussions with the PDG and NICE on 20th July 2010, a number of the above interventions were deemed to be unsuitable for a community-based intervention. Only interventions 1,3,5,6 and 9 have therefore been included in the modelling.

These interventions have only been evaluated in the specific cohorts that they were studied, eg low SES.

2.2.1.1. Strength of the evidence

It should be noted that we were able to obtain the confidence intervals around outcomes for some of the smaller studies, and these generally indicated a lack of statistical

significance as illustrated by the confidence intervals around the outcomes in the Ashfield-Watt study in Table 9 below**.** This is not surprising given that studies often have small number of patients, that there is considerable patient variability in response, and that the mean effects were small.

Table 9 : Ashfield-Watt - Change in daily fruit & veg intakes

		Control			Intervention		
		Mean	95% CI lower limit	95% CI upper limit	Mean	95% CI lower	95% CI upper
Total fruit & veg	Baseline	5.6	1.484	9.716	4.8	0.684	8.916
	Follow-up	5.1	0.984	9.216	4.6	0.484	8.716
	Change	-0.4	-4.516	3.716	-0.1	-4.216	4.016

It should also be remembered that there is considerable uncertainty around how successfully interventions tested in small pilots would actually be in clinical practice.

Studies reporting behavioural outcomes are often based on crude self-reported data, at one point in time. This also weakens the strength of any evidence synthesis based on this data.

2.2.2. What-if scenarios

Set out in Table 11 below are what-if scenarios to illustrate the potential cost-effectiveness of hypothetical interventions of alternative degrees of effectiveness and unit cost, modelled in alternative subgroups of the population. The default assumption about weight regain is by the end of year 3 (see Section 2.3 below).

For these what-if scenarios, the unit cost represents a 'package' cost, i.e. it is the whole cost of the initial and any subsequent maintenance intervention (to be spread out across years as deemed appropriate by policy-makers).

Given the uncertainty around the rate of weight regain, a further set of sensitivity analyses have been undertaken assuming that weight is regained –

a) over a period of 6 years from the intervention
b) during the first year such that there is no benefit after that

Table 10 : Proposed interventions scenarios based on evidence from studies

Intervention	Based on studies	Study settings (BME / SES / Obese)	Effectiveness	Estimated Cost per individual
1. Dietary/nutritional - fruit and vegetable intake	Ashfield-Watt, Bremner	Low SES	BMI : 0 (see note 1) SBP : -0.10 TC/HDL : -0.4%	£ 42
2. Dietary/nutritional – behavioural counselling	Steptoe	Low SES	BMI : -0.04 SBP : -0.24 TC/HDL : -0.4%	£ 59
3. Dietary/nutritional – broad dietary education/cooking skills	Wrieden 2006, McKellar	Low SES	BMI : -0.60 SBP : -2.35 TC/HDL : +3.8%	£ 75
4. Physical activity – exercise consultation	Lowther	Low SES	Negative study (BMI not reported but did not result in increase in physical activity in minutes per week)	
5. Opening of a new food retail outlet	Cummins 2005,	Low SES	BMI : 0 (see note 1) SBP : -0.06 TC/HDL : -0.2%	Indeterminable. To be explored using threshold analysis
6. Multi-component – small scale	Gray	Low SES	BMI : -1.29	£ 180
7. Access to an internet portal	Lindsay	Low SES	Negative study (BMI not reported but did not result in increase in days/week of moderate exercise)	
8. Workplace counselling	Proper	Assumed obese	BMI : -0.22 TC /HDL : -3.3%	430 euros

9. Large-scale, region-wide multi-component (like Hartslag Limburg)	Schuit	Low SES subgroup	BMI : -0.27 SBP : -6.1 TC/HDL : -0.8% HDL : +0.02	4 euros
10. Mass media campaign	OECD	Assumed obese	BMI : 0 (see note 1) SBP : -0.18 TC/HDL : -0.6%	$ 2.27
11. Fiscal measures	OECD	Assumed obese	BMI : 0 (see note 1) SBP : -0.09 TC/HDL : -0.3%	$ 0.28
12. Food advertising regulation	OECD	Assumed obese	BMI : -0.15	$ 7.11
13. Food advertising self-regulation	OECD	Assumed obese	BMI : -0.48	$ 0.51
14. Food labelling	OECD	Assumed obese	BMI : -0.02	$ 3.18

BMI and SBP are absolute changes; Effect on TC:HDL ratio shown as percentage change

Note 1

Furthermore some interventions were purely analyses of the HSE data-based interventions suggesting that increased fruit and vegetable may result in a slight increase in BMI but this may be due to an absence of calorie control (which could not be adjusted for in the analyses). In reality, recommendations on fruit and vegetable intake are likely to be made within a broader set of dietary recommendations which should promote weight control. **Therefore, for interventions where BMI is not reported but fruit and vegetable intake is, we have assumed no BMI change for the purpose of the modelling.**

Note 2

Only interventions 1,3,5,6 and 9 have therefore been included in the modelling (see section2.2.1 above)

Note 3

Evidence for the effectiveness and cost of the Large-scale, region-wide multi-component (Intervention 9) came from separate sources. The study design for this programme was with a reference region as the 'comparator'. The blood pressure results also seem to be quite large relative to the BMI change, especially when set against the cost per individual of 4 euros. We are seeking confirmation that there is consistency between our identified costs and effectiveness for this intervention.

Table 11 : What-if scenarios with alternative effect sizes in different subgroups

Scenarios for effect size	None	A. Very Small	B. Small	C. Moderate	D. Substantial	E. Large
BMI	0	-0.1	-0.3	-0.5	-1	-1.5
SBP	0	-0.3	-0.8	-1.3	-2.7	-4
TC:HDL	1.000	0.998	0.994	0.990	0.980	0.970
Unit cost of intervention assumed (per person)						
i)		£ 1	£ 1	£ 1	£ 1	£ 1
ii)		£ 10	£ 10	£ 10	£ 10	£ 10
iii)		£ 100	£ 100	£ 100	£ 100	£ 100
iv)		£ 1000	£ 1000	£ 1000	£ 1000	£ 1000
Obese criteria applicable						
a) obese only				Y		
b) any BMI	Y	Y	Y	Y	Y	Y

Population Mix (No BMI criteria)	**England Average**	**Deprived Locality with average ethnicity**	**High Ethnic Locality with average deprivation**	**High Ethnic High Deprived**	**High Ethnic (All Asian) High Deprived**	
%SES	18%	50%	20%	50%	46%	see note 1
%BME	10%	11%	52%	52%	53%	see note 1
%Asian	6%	5%	29%	29%	53%	see note 1

No BMI restriction has been applied for either the intervention scenarios or the what-if scenarios on the grounds that interventions are offered to a community, so any individuals may participate. Experience also indicates that differential uptake may not be towards those with the greatest need so those with lower baseline BMI may be equally likely to participate as obese individuals. An additional what-if analysis was undertaken to assess cost-effectiveness in the obese only sub-group (for the moderate intervention – intervention C).

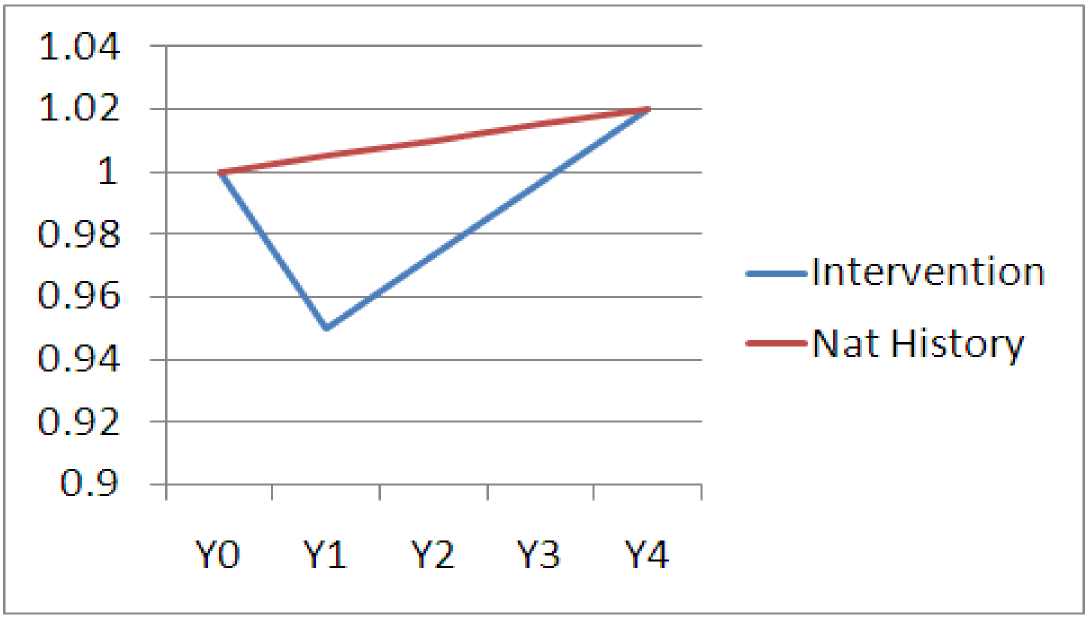
2.3. Evidence for durability of effects and weight regain

Weight loss is often difficult to sustain for many people in the long-term, especially without an on-going maintenance intervention for a few years. Assumptions about rate of regain need to be consistent with assumptions about the existence or otherwise of any on-going maintenance intervention.

For the model, we decided that the best approach to determine intervention-specific rates of weight regain is based on the time to revert to the natural history level (rather than assuming that the rate of regain is the same for any intervention). This is because where interventions achieve a large initial weight loss, the rate of regain is likely to be greater.

We have assumed in the base case that weight (and BMI) is gradually regained after the intervention such that in year 4 of the model (from the start of the intervention), BMI has returned to the trajectory of control patients, i.e. those not receiving any intervention (as illustrated below).

Figure 3 : Example BMI trajectory with intervention and control



This is judged as a reasonable assumption in between more extreme assumptions based on:

a) Evidence of rapid weight regain within a year or two in the absence of any surveillance especially the early attempts at adapting intensive RCTs of diabetes prevention programmes to real-world settings (Yates et al. Primary Care Diabetes 2007), and
b) a meta-analysis of evidence from trial settings (of possibly highly motivated individuals with on-going surveillance) that only 50% of weight is regained within 3 years (Dansinger et al. Ann Intern Med. 2007).

In order to obtain benefits beyond the year of the intervention, it may be desirable to put in place some means of follow-up sessions to monitor individuals' progress and encourage people to sustain behavioural changes. The number of intervention contacts with subjects, a key driver of the cost of intervention, has been shown to be significantly correlated with weight loss[14]. We have therefore assumed that interventions might be accompanied by some additional monitoring or follow-up sessions after the intervention. For the analyses, we therefore present results with alternative assumptions for the extent of on-going maintenance during the period in which a BMI reduction is partially sustained. For illustration, we have used 3 scenarios for this, equivalent to the costs of 0, 1 and 2 visits to a nurse per year (each one costing £9.64 based on a 15 minute consultation – Curtis 2009). In practice, on-going support could be provided by alternative means such as internet or email communication, or possibly lay-worker led group meetings.

We assume that changes in blood pressure and lipids arising from intervention also reverse in the same timescale as weight regain.

2.4. Cost-effectiveness Evidence review

2.4.1. Search strategy for UK-based evidence

Studies were identified through the review search strategies. The mapping review search strategies, as shown in detail in Appendix 1, were also used to search specific economic databases: NHS Economic Evaluation Database (via Wiley) and EconLit (via OVID SP). The Public Health Interventions Cost Effectiveness Database (PHICED) which is part of the National Library for Public Health was also searched using the limits of public health area: obesity or physical activity.

The search did not identify any UK-based evidence that could be used to inform the modelling.

In addition, previous NICE guidance on Obesity and Physical Activity was also reviewed, and, to the above, building on the ScHARR team's existing knowledge of the relevant literature, further relevant literature was identified using searching in the form of citation searching, and reference tracking.

2.4.2. NICE Obesity Guideline modelling

Chapter 16 of this guidance on the economics of public health interventions was reviewed to identify potential relevant studies and to obtain cost-effectiveness estimates. None of the studies reported in this document met the criteria for being a suitable community-based intervention.

2.4.3. Foresight model

The work completed by the FORESIGHT group[15] was reviewed. This helped to inform the areas of focus for further development of the decision-analytic model, especially the inclusion of the costs of osteoarthritis because of the high cost burden (comparable with the cost of diabetes). The impact of the method for forecasting future BMI trends also directed us towards alternative scenarios for these trends as they are uncertain. In particular, current trends may not persist in the medium term. We have also included some aspects that were not included in the FORESIGHT work, for example the impact of socioeconomic status on risk of CVD and diabetes.

2.4.4. Economic analyses specifically assessing Physical Activity interventions

NICE Guidance on "Four commonly used methods to increase physical activity: brief interventions in primary care, exercise referral schemes, pedometers and community-based exercise programmes for walking and cycling" did not identify any strong evidence on community-based exercise schemes. Across all scenarios, in all four methods, the future discounted costs saved exceed intervention cost per participant. Benefits accrued range from 0.07 – 1.15 QALYs gained per person[16].

In production of the NICE Guidance on 'Physical Activity and the environment'[17], review efforts encountered difficulties with interpretation of study results and generalisability to other settings. The associated economic analysis[18] estimated that an urban trail would have an ICER in the range £130 to £25,000 per QALY and a mean estimated cost-benefit ratio of 1:11 for cycling infrastructure also suggests this may be cost-effective.

Underpinning NICE guidance on ‘Promoting physical activity in the workplace’, an economic analysis was undertaken. The guidance reports that, overall, workplace physical activity counselling and fitness programmes were found to be cost effective. In addition, the introduction of a workplace physical fitness programme may be broadly beneficial to employers in that it can help reduce absenteeism[19].

Similar conclusions were arrived at in another review, although there was a suggestion that some interventions can increase physical activity “at reasonable costs”[20]. In particular a pedestrian/bicycle trail is a community intervention which has been estimated to have a incremental cost-effectiveness ratio of approximately 10 000 Euros.

Annemans et al (2007) built a transition state model to investigate the impact of physical activity in a fitness centre environment on 3 different cohorts. Results of this Belgian study show clear advantages for physical activity versus inactivity, with an ICER in the range of €2,000-15,000/QALY depending on risk profile of the cohort.

Cobiac et al (2009) assessed the cost-effectiveness of 6 different interventions for promoting physical activity in Australia. Apart from general practitioner referral to an exercise physiologist, all interventions were cost-effective at the $50,000/DALY mark. Furthermore, programmes that encourage the use of pedometers and mass media-based community campaigns were proved to be dominant (i.e. less expensive and greater benefit than usual care) across all scenarios.

Physical activity interventions in general seem to offer a cost-effective option but cultural and other barriers relating to BME and low SES groups needs to be taken into account.

Evidence has recently begun to emerge on the beneficial effects of physical activity on kidney function (Robinson-Cohen et al, 2009) although there is not enough evidence to justify inclusion in the model.

Marcus et al reviewed studies on mass media interventions for physical activity behaviour change. This concluded that people generally remembered the message of the intervention but there was little evidence for actual change in behaviour[21].

2.4.5. Cost-effectiveness of other studies identified

Bemelmans reported that a programme combining a community component based on the Hartslag Limburg programme and an intensive programme for some individuals is very cost effective at €5700 per QALY gained[6].

2.5. Economic Model Overview

A health-state transition model was developed in Excel spreadsheet software with Visual Basic for Applications (VBA) programming.

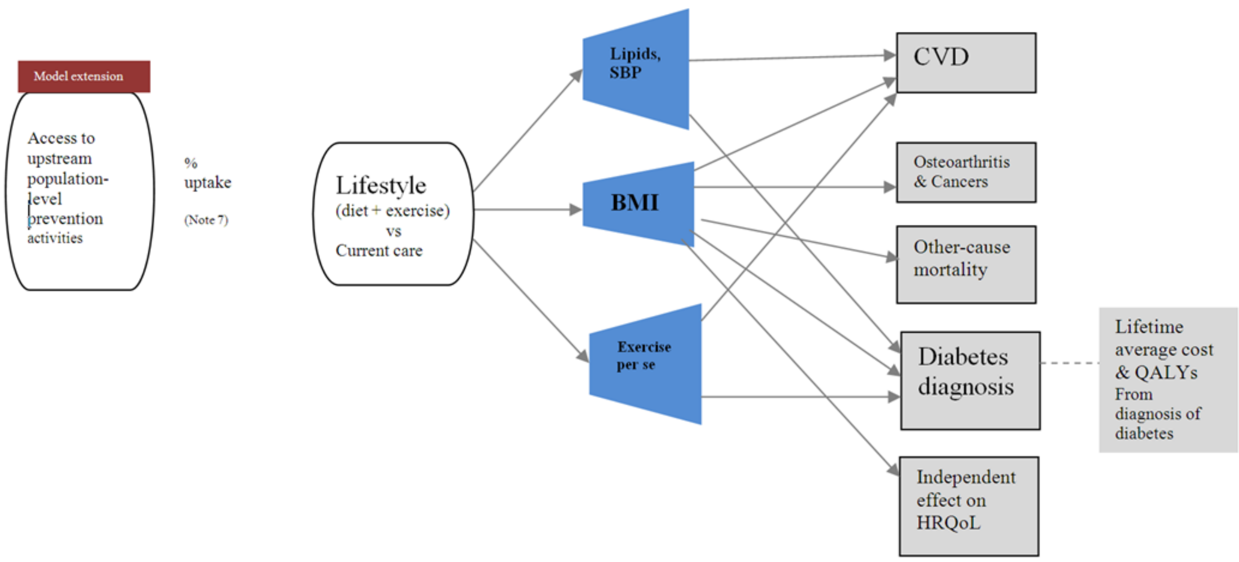
The model predicts transitions between health states on an annual cycle using transition probabilities obtained from algorithms such as QRISK®2 and QDScore®. The model allows clinical, cost and quality-of-life outcomes from proposed treatment strategies to be simulated and compared over a lifetime with alternative treatment strategies or with usual care.

The decision-analytic approach using Markov-based sub-models for CVD, diabetes etc enables the impact of 'competing risks' on diluting the benefit of interventions to be taken into account.

For each scenario, annually updated risk factor values for the QRISK®2 and QDScore® algorithms were calculated from baseline levels, initial intervention effects and any subsequent loss of effect, and the underlying natural history of the risk factors. The intervention arm used data from the case studies to model the predicted effects of the proposed interventions. The rates at which effects of intervention are lost are either based on specific follow-up data quoted in the studies, or based on general assumptions based on relevant literature.

2.6. Economic Model schematic

Figure 4 : Model schematic



2.7. Baseline characteristics data and Subgroups of interest

2.7.1. Health Survey for England Database[22]

For modelling the baseline population, it was decided to use data from the most recently available (2008) Health Survey for England (HSE). This survey provided a representative sample of 15102 adults, and in that year included extra questions relating to diet and exercise. For each individual, data on risk factors relating to CVD and type 2 diabetes were extracted to produce a simulation cohort with characteristics that reflected overall population parameters.

The HSE consists of over 2200 responses to questions and derived measures, and as it would be impractical to obtain all details for the entire sample, a number of questionnaire booklets are produced and applied to various sub-groups. Because of this survey design, most individuals would not have details for the complete set of risk factors required for the QRISK®2 and QDScore® algorithms, and it was therefore necessary to impute the missing values.

If details were obtained from a group of survey participants, then these values were used as the basis for assigning missing values, while for those risk factors not addressed by the HSE their prevalence in the general population was used. Age and gender were recorded for the entire survey group.

Where values for BMI, systolic blood pressure or HDL:cholesterol ratio were missing (15%, 40.6%, and 58.6% respectively), a value was randomly sampled from the distribution characteristics of all those individuals of the same age and gender for whom data were available. This compares with the web-based QRISK®2 and QDScore® approach, which is to use a fixed default value based on age-gender averages.

The remaining parameters in QRISK®2 and QDScore® are entered according to the presence or absence of each risk factor. Where this was recorded for a sub-group in the HSE, the prevalence in that sub-group was used to assign a value for the remainder. Smoking habits were obtained from a sub-group of 10739 people representing 71% of the sample. Of these 20% were current smokers, and so the remaining individuals were each given a 20% chance of being assigned that risk factor. In the same way, 2833 (18.8%) people were asked about heart problems of whom 33 had experienced atrial fibrillation. This translates to a corresponding sample prevalence of 1.2%. For hypertension, the sub-group size was 5709 (37.8%) and the prevalence was 32.5%. This risk factor was significantly age related, however, and so the age distribution was taken into account when assigning it to individuals. If the risk factor was not addressed at all by the HSE, the case for all the remaining parameters, the population prevalence was used instead.

2.7.2. Mapping HSE Social Economic Group data to Townsend Scores

Townsend scores, a measure of area deprivation, were not included in the HSE data set, and so a value derived using an individual's Social Economic Group (SEG) as a proxy. Using data from the 2001 census, the University of Manchester has produced Townsend scores for 8844 Electoral Wards in England[23]. These scores ranged from -4.95 to +20.67 with a median value of -1.05; higher values indicating greater deprivation. The scores were ranked, and then grouped to match the proportion of people in each of the six standard SEGs. Townsend scores were then assigned to each individual by sampling random percentiles from the Ward group corresponding to their SEG. In those few cases where SEG was not recorded (3.3%), the average Townsend score of zero was used.

The results of this mapping exercise are summarised in Table 12 below.

Table 12 : Social class to Townsend score mapping

Social Class		% of HSE population	Townsend score range
I	Professional	6.9	-4.95 to -3.36
II	Managerial/technical	36.5	-3.36 to -1.46
IIIN	Skilled, non-manual	15.7	-1.46 to -0.35
IIIM	Skilled manual	22.7	-0.35 to 2.5
IV	Semi-skilled manual	13.5	2.5 to 7.01
V	Unskilled manual	4.7	7.01 to 20.67

For our purposes we have treated Classes IV and V as low SES although an intervention with a broader coverage might also target as considerable proportion of class IIIM.

A sample of 15102 simulated individuals, with risk characteristics as far as possible being based on the HSE primary data, was thus produced for use in the model.

2.7.3. Identification of cohorts of most interest for the modelling

Black and Minority Ethnic sub-populations are known to be at high risk for progression to pre-diabetes and development of CVD. These factors per se may account for excess risk but this may also be partly attributable to raised risk factors for CVD and diabetes.

Low socioeconomic status groups are also at higher risk than the overall population but there is likely to be considerable variation even within categories defined within the HSE. A preliminary analysis of the HSE database could be used to help refine criteria for targeting specific high-risk sub-populations within low socioeconomic status groups.

The general obese population might be of interest (i.e. BMI>30 for whites and >27.5 for BME groups)

Equally, there may be other sub-populations, e.g. older age groups, that do not fall within the BME and low SES sub-population, that are at high risk of CVD or Type 2 diabetes. The benefit of intervention in such groups is unclear – modelling can help to quantify the trade-off between the opposing influences on cost-effectiveness, i.e. such populations may indeed be at high risk but are only able to derive shorter duration of benefit compared to younger age groups. It is possible to analyse the HSE data in order to present the distribution of risk of CVD or Type 2 diabetes (amongst the sub-population not falling into either the BME and low SES categories) in order to potentially assist the PDG in specifying criteria for another subgroup of interest.

Baseline characteristics for the particular socioeconomic status, BME, and potentially other, groups of interest will be extracted from the HSE dataset and entered into the QRISK®2 and QDScore® algorithms in order to quantify the extent to which their risk of CVD or Type 2 diabetes differs from that of the rest of the sample.

For the simulation model, cohorts for each high-risk group will be generated by filtering the relevant individuals from the HSE dataset.

2.8. Natural History - BMI, SBP and lipids

Inclusion of the underlying natural history is important because the non-linear relationship between BMI and CVD risk means that the natural history assumptions affects the absolute difference in risks between treatment groups. For example, the difference in outcomes between a BMI level of 40 versus 35 will not be the same as a BMI of 35 versus 30. It is unclear if omission of these would lead to an under or over-estimate of cost-effectiveness. This depends on the relative impacts of –

- Higher BMI and SBP trends increasing the absolute risks of CVD events and hence the differential between treatment arms
- Higher BMI and SBP trends lead to increased mortality, thereby lowering the benefit of intervention

Alternative options for the change in BMI without intervention identified from the literature include –

i) FORESIGHT-based approach: based on Health Survey for England data and forecasting assumptions resulting in a logarithmic-shaped trajectory (i.e. tailing off over time)

ii) Simple increase :
  a. 0.26 BMI/ annum (Macdonald 1997[24]) or
  b. 1kg per annum (Heitman 1999)

iii) 'Steady state', i.e. no increase, is simplest approach and an assumption made in a lot of economic studies[25]. This potentially could lead to slightly inaccurate differences in predicted outcomes between study arms (but it is difficult to say whether underestimated or overestimated)

Recent UK Guidelines for Obesity state that BMI increases with age and analysis from the Health Survey for England (HSE) shows a quadratic relationship between BMI and age for both sexes[25].

Our plan is to model two scenarios – one with a steady state and one with an annual increase (logarithmic shape tailing off over time).

2.9. Modelling the impact of lifestyle changes on obesity, diabetes, CVD, and other co-morbidities

2.9.1. CVD

2.9.1.1. First event (QRISK®2 algorithm)

Like other CVD risk algorithms, QRISK®2 estimates an individual's annual risk of suffering a cardiovascular event based on a number of personal risk factors. QRISK®2 was considered the preferred algorithm for risk of CVD as it is UK-based and because it has been shown to offer improved prediction of a patient's 10-year risk of cardiovascular disease over the NICE version of the Framingham equation[26].

The outcomes include heart attack, angina, stroke or transient ischaemic attack (TIA) but not peripheral vascular disease.

The input parameters differ slightly between the QRISK®2 CVD and QDScore® diabetes algorithms, and are listed in Table 13

Table 13 : Input parameters for QRISK®2 and QDScore®

Input parameter	QRISK®2	QDScore®
Age	X	X
Body mass index	X	X
Townsend score	X	X
Systolic blood pressure	X	
Total : HDL Cholesterol ratio	X	
Family history of coronary heart disease	X	
Smoker	X	X
Treated hypertension	X	X
Type 2 diabetes	X	
Atrial Fibrillation	X	
Rheumatoid arthritis	X	
Chronic renal failure	X	
History of cardiovascular disease	X	X
Ethnicity	X	X
Gender	X	X
Steroids		X
Family history of diabetes		X

The advantage of using these equations in this model is that they explicitly include risk factors associated with groups of specific interest, that is, socio-economic status - via Townsend score, and ethnicity.

The 9 categories of ethnicity are –

White	Black Caribbean	Indian
Pakistani	Chinese	Bangladeshi
Black African	Other Asian	Other ethnic group

2.9.1.2. Secondary CVD event rates

Rates of subsequent events (MI and stroke) have been reported from the province of Saskatchewan, Canada, all of whom had had an index event[27]. Rates of secondary myocardial infarction, stroke including intracranial haemorrhage, or death occurred at a rate of 15.9 per 100 patient-years.

The algorithm was incorporated into the model using the open source code [28].

2.9.1.3. Split of CVD events into type of event

Events were split into coronary events and stroke events using reported incidence in the dataset underpinning the QRISK®2 algorithm {139}. Events were further split into stable angina, unstable angina, non-fatal MI, fatal MI, transient ischaemic attack or fatal stroke using splits reported in an HTA assessment of statin therapy [19].

The model includes no relationship between SBP or BMI and CVD case fatality rates as we are unaware of any evidence for such a relationship. Similarly no relationship between socioeconomic status or ethnicity is incorporated into the case fatality rates.

2.9.1.4. Effect of intervention on risk of CVD

BMI

No evidence exists from controlled intervention studies, to our knowledge, showing the effect of changes to BMI etc on hard outcomes such as CVD.

SBP

Blood pressure is known to be a causal factor for CVD but estimates of the relative risk reduction seem very mixed, indeed QRISK®2 includes a variable for treated hypertension which effectively multiplies the risk of CVD by 1.5, ie your risk at an SBP of 130mmHg on treatment is not the same as if it had always been at that level.

TC:HDL

Regarding lipid changes, no evidence exists to show that raising HDL reduces risk.

Overall approach

Given the above uncertainties and limited evidence, we decided that attempting to obtain an alternative approach to that of using associations within QRISK®2 to predict the benefit of intervention would be complex and relatively unproductive.

2.9.2. Diabetes – QDScore®

Baseline risk :

As the approach used to construct the QRISK®2 equation for CVD has been shown to be robust, we chose the QDScore[29] for the estimation of risk of developing Type 2 diabetes as it is based on the same dataset and methodology. The variables included in QDScore® are shown in Table 13 above.

The open source code for the QDScore® algorithm was obtained from the ClinRisk website [16].

Effect of intervention on risk of diabetes :

Evidence from the large Finnish Diabetes Prevention Study and American Diabetes Prevention Study suggests that each unit BMI reduction leads to an estimated 34% reduction in risk of developing Type 2 diabetes (Lindstrom 2005, Hamman 2006). This is much higher than the 19% epidemiological association within the QDScore® algorithm. One caveat is that patients in these large prevention trials were at high risk of diabetes at baseline (although our model cohort is also probably at high risk over a long time horizon).

2.9.3. Osteoarthritis, Obesity-related cancers and other conditions

The cost of these diseases has been incorporated into the modelling by applying an uplift of 1.59 to the costs arising from CVD and diabetes. The basis of this is shown in **Table 14** below (figures obtained from Tim Marsh, National Heart Forum).

Table 14 : Uplift to account for costs of osteoarthritis, obesity-related cancers and other conditions

Year	**2040**
chd	5.42
stroke	6.23
diabetes	4.1
Sum Vascular	15.75
hypertension	0.64
gall-bladder disease	0.13
arthritis	6.34

breast cancer	0.26
colorectal cancer	0.53
endometrial cancer	0.13
kidney cancer	0.16
liver cancer	0.94
oesophageal cancer	0.22
Sum Non-Vascular	9.35
Uplift for non-vascular	1.59

We have not modelled the detailed disease natural history or quality-of-life for these other illnesses.

2.9.4. Other-cause Mortality

Mortality from other causes were based on published life-tables[28].

2.9.5. Effect of exercise on CVD risk and diabetes independent of BMI

20% of coronary heart disease (CHD) and 10% of stroke in developed countries is due to physical inactivity [3].

In the WHO Global strategy on diet, physical activity and health (2004), it is asserted that there are additional health benefits to be gained from physical activity that are independent of nutrition and diet.

We have been unable to incorporate exercise effects as were unable to identify a multivariate equation for exercise alongside other risk factors (such as socioeconomic status and ethnicity) for CVD or diabetes.

2.10. Health State Costs

As first-year costs associated with cardiovascular events are significantly greater than the subsequent costs of continuing care, the health states included in the model distinguished between subjects suffering an event in the current year, and those who, although having no further CVD events in the current year, had a history of established CVD. Most unit costs for CVD events are based on a publication from the UKPDS study(UKPDS65). The lifetime cost of Type 2 diabetes, adjusted for age at diagnosis, was derived from previous published modelling of diabetes within ScHARR (Waugh 2007). The cost for someone diagnosed at age 50 was estimated to be £16,846.

[3] BHF National Centre – Physical Activity and Health, http://www.bhfactive.org.uk/downloads/Economics%20factsheetD.pdf

2.11. Utility scores

Health-related quality-of-life (HRQoL) is typically measured on a scale of 0 (dead) to 1 (perfect health) and reported as a utility score.

Baseline utility values were obtained from the EQ5D scores within the Health Survey for England dataset. For CVD events and co-morbidities such as heart attacks, utilities were mainly sourced from UKPDS62 (Clarke 2002) and Coffey 2002.

The effect of weight on utility, estimated from the Health Survey for England dataset, is a decrement of 0.005 per unit increase in BMI.

2.12. Other Assumptions

Horizon :

The model horizon used was 80 years (effectively lifetime).

Perspective :

For NICE Public Health modelling, a Public Service perspective is appropriate but as the relevant costs are mainly health service costs, the perspective is effectively that of health and social care. Specifically, indirect costs (for example time off work) are not included.

2.13. Timing and duration of benefits

The Jarrett article [4] also re-enforces doubts about the size of benefits that would be realised from short-term changes in BMI.

[4] Sourced from 'Are obesity related diseases and conditions really 'a myth'?' at http://www.diabetes.org.uk/About_us/News_Landing_Page/Are-obesity-related-diseases-and-conditions-really-a-myth/

3. RESULTS

3.1. Interventions with Direct Evidence in Low SES Groups

Five interventions based directly on specific published studies have been modelled, each in a population group consisting entirely of in low SES (the target group in the studies concerned). The results for each are summarised below.

The results presented below are deterministic, i.e. we have not included parameter uncertainty in the modelling (using Probabilistic Sensitivity Analysis). The comments on the strength of the evidence base in Section 2.2.1.1, and the study sample sizes shown in Sections 2.1.1 and 2.1.2, should therefore be borne in mind when interpreting these results.

Overall cost-effectiveness is reported as the incremental cost-effectiveness ratio (ICER) which is calculated as incremental costs (intervention less control) divided by incremental QALYs gained (intervention less control). Interventions with a ratio below £ 20,000 per QALY are deemed to be cost-effective**. However, where either (or both) of incremental costs or incremental QALYs gained are negative, the above rule of interpretation of the ICER is not applicable.** In such cases, we state next to the calculated ratio whether the intervention is cost-effective at a £ 20,000 per QALY threshold. Where incremental costs are negative (i.e. intervention is cost-saving) and incremental QALYs are positive, the intervention is said to be 'dominating' (the control arm) in addition to being cost-effective. Where incremental costs are positive and incremental QALYs are negative, the intervention is said to be 'dominated' (by the control arm).

Table 15: Intervention 1 (Dietary / Nutritional – Fruit & Veg Intake)

Intervention	Education to promote increased fruit and vegetable intake		
Studies used	Ashfield-Watt et al, Bremner et al		
Direct Cost per Participant (Y1)	£46.33		
Mean Benefits (Y 1) versus control			
BMI	0.000		
SBP	-0.100		
TC:HDL	0.996		
Estimated Incremental Cost-Effectiveness for the Cohort over the lifetime (per person)			
	Intervention	Control	Difference
Direct Costs of Intervention	£44	£0	£44
Lifetime Costs of Complications	£11,072	£11,072	£0
Total Costs (Discounted)	£11,116	£11,072	£44
Lifetime QALYs (Discounted)	11.5185	11.5185	0.0000
Incremental Cost per QALY	**Not cost-effective**		
Sensitivity Analysis on additional (over and above current) follow up from NHS			
	Inc Cost	Inc QALY	**Incr. Cost per QALY**
0 practice nurse visits	£44	-	**Not cost-effective**
3 practice nurse visits (1 per year)	£62	-	**Not cost-effective**
6 practice nurse visits (2 per year)	£89	-	**Not cost-effective**
Threshold support cost if intervention is to be considered cost-effective			
Total Support Package: Cost Threshold	N/A		

Table 16: Intervention 3 (Dietary / Nutritional – Broad Dietary Education / Cooking Skills)

Intervention	Dietary/nutritional – broad dietary education/cooking skills		
Studies used	Wrieden et al, McKellar et al		
Direct Cost per Participant (Y1)	£85.21		
Mean Benefits (Y 1) versus control :			
BMI	-1.040		
SBP	-2.350		
TC:HDL	1.038		
Estimated Incremental Cost-Effectiveness for the Cohort over the lifetime (per person)			
	Intervention	Control	Difference
Direct Costs of Intervention	£82	£0	£82
Lifetime Costs of Complications	£11,002	£11,072	*-£70*
Total Costs (Discounted)	£11,084	£11,072	£11
Lifetime QALYs (Discounted)	11.5314	11.5185	0.0129
Incremental Cost per QALY			**£878**
Sensitivity Analysis on additional (over and above current) follow up from NHS			
	Inc Cost	Inc QALY	**Incr. Cost per QALY**
0 practice nurse visits	£11	0.0129	**£878**
3 practice nurse visits (1 per year)	£29	0.0129	**£2,252**
6 practice nurse visits (2 per year)	£56	0.0129	**£4,350**
Threshold support cost if intervention is to be considered cost-effective			
Total Support Package : Cost Threshold	£172		

Table 17: Intervention 5 (Opening of a New Food Retail Outlet)

Intervention	Opening of a new food retail outlet		
Studies used	Cummins et al		
Direct Cost per Participant (Y1)	£0.00		
Mean Benefits (Y 1) versus control			
BMI	0.000		
SBP	-0.060		
TC:HDL	0.998		
Estimated Incremental Cost-Effectiveness for the Cohort over the lifetime (per person)			
	Intervention	Control	Difference
Direct Costs of Intervention	£0	£0	£0
Lifetime Costs of Complications	£11,072	£11,072	£0
Total Costs (Discounted)	£11,072	£11,072	£0
Lifetime QALYs (Discounted)	11.5185	11.5185	0.0000
Incremental Cost per QALY			**Not cost-effective**
Sensitivity Analysis on additional (over and above current) follow up from NHS			
	Inc Cost	Inc QALY	**Incr. Cost per QALY**
0 practice nurse visits	£0	0.0000	**Not cost-effective**
3 practice nurse visits (1 per year)	£18	0.0000	**Not cost-effective**
6 practice nurse visits (2 per year)	£45	0.0000	**Not cost-effective**
Threshold support cost if intervention is to be considered cost-effective			
Total Support Package : Cost Threshold	£0		

Table 18: Intervention 6 (Multi-Component Small Scale)

Intervention	Multi-component – small scale		
Studies used	Gray et al.		
Direct Cost per Participant (Y1)	£185.40		
Mean Benefits (Y 1) versus control			
BMI	-1.290		
SBP	0.000		
TC:HDL	1.000		
Estimated Incremental Cost-Effectiveness for the Cohort over the lifetime (per person)			
	Intervention	Control	Difference
Direct Costs of Intervention	£179	£0	£179
Lifetime Costs of Complications	£10,971	£11,072	*-£101*
Total Costs (Discounted)	£11,150	£11,072	£78
Lifetime QALYs (Discounted)	11.6565	11.5185	0.1380
Incremental Cost per QALY			**£562**
Sensitivity Analysis on additional (over and above current) follow up from NHS			
	Inc Cost	Inc QALY	**Incr. Cost per QALY**
0 practice nurse visits	£78	0.1380	**£562**
3 practice nurse visits (1 per year)	£95	0.1380	**£690**
6 practice nurse visits (2 per year)	£122	0.1380	**£886**
Threshold support cost if intervention is to be considered cost-effective			
Total Support Package : Cost Threshold	£2,574		

Table 19: Intervention 9 (Large scale region-wide multi component)

Intervention	Large-scale, region-wide multi-component (like Hartslag Limburg/Schuit)		
Studies used	Schuit et al.		
Direct Cost per Participant (Y1)	£3.84		
Mean Benefits (Y 1) versus control			
BMI	-0.270		
SBP	-0.610		
TC:HDL	0.992		
Estimated Incremental Cost-Effectiveness for the Cohort over the lifetime (per person)			
	Intervention	Control	Difference
Direct Costs of Intervention	£3	£0	£3
Lifetime Costs of Complications	£11,050	£11,072	*-£22*
Total Costs (Discounted)	£11,053	£11,072	*-£19*
Lifetime QALYs (Discounted)	11.6451	11.5185	0.1266
Incremental Cost per QALY			***-£153*** (cost-effective and dominating)
Sensitivity Analysis on additional (over and above current) follow up from NHS			
	Inc Cost	Inc QALY	**Incr. Cost per QALY**
0 practice nurse visits	-£19	0.1266	***-£153*** (cost-effective and dominating)
3 practice nurse visits (1 per year)	-£2	0.1266	***-£13*** (cost-effective and dominating)
6 practice nurse visits (2 per year)	£25	0.1266	**£200**
Threshold support cost if intervention is to be considered cost-effective			
Total Support Package : Cost Threshold	£2,528		

3.2. What-If Scenarios for Interventions of Illustrative Effectiveness in Different Target Cohorts

Five scenarios for interventions have been modelled with effectiveness in the first year ranging through very small, small, moderate, substantial and large (see Table 11). Each has been modelled versus a control with zero effect. The results are summarised in the 5 different illustrative cohorts below.

Table 20 Cohort Definitions

Main Cohorts for Analysis	Obese Cohorts used for sensitivity analysis
18+, **Any BMI**, Not already got diabetes or CVD	18+, **BMI over 30**, Not already got diabetes or CVD
1. England Average	OB1. England Average
2. Deprived /Average BME	OB2. Deprived /Average BME
3. Average Deprivation /High BME	OB3. Average Deprivation /High BME
4. Deprived /High BME	OB4. Deprived /High BME
5. Deprived /High Asian	OB5. Deprived /High Asian

Table 21 Effectiveness in terms of Average QALYs Lived by Effect Size and by Cohort

INTERVENTION A: Very small BMI=-0.1 , SBP=-0.3, TC:HDL =.998	Intervention QALYs (Discounted)	Control QALYs (Discounted)	QALY Difference
1. England Average	12.4526	12.4514	0.0012
2. Deprived /Average BME	11.7956	11.7945	0.0011
3. Average Deprivation /High BME	11.9769	11.9751	0.0018
4. Deprived /High BME	11.5018	11.5013	0.0005
5. Deprived /High Asian	10.5606	10.5610	-0.0004
INTERVENTION B: Small effect BMI=-0. 3, SBP=-0.8, TC:HDL =.994			
1. England Average	12.4557	12.4514	0.0043
2. Deprived /Average BME	11.7983	11.7945	0.0037
3. Average Deprivation /High BME	11.9803	11.9751	0.0052
4. Deprived /High BME	11.5042	11.5013	0.0029
5. Deprived /High Asian	10.5634	10.5610	0.0024
INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990			
1. England Average	12.4591	12.4514	0.0077
2. Deprived /Average BME	11.8018	11.7945	0.0072
3. Average Deprivation /High BME	11.9835	11.9751	0.0084
4. Deprived /High BME	11.5063	11.5013	0.0051
5. Deprived /High Asian	10.5661	10.5610	0.0051
INTERV'N D:Substantial effect BMI=-1.0 , SBP=-2.7, TC:HDL =.980			
1. England Average	12.4686	12.4514	0.0172
2. Deprived /Average BME	11.8071	11.7945	0.0126
3. Average Deprivation /High BME	11.9904	11.9751	0.0153
4. Deprived /High BME	11.5154	11.5013	0.0141
5. Deprived /High Asian	10.5710	10.5610	0.0100
INTERV'N E: Large effect BMI=-1.5 , SBP=-4.0, TC:HDL =.970			
1. England Average	12.4776	12.4514	0.0261
2. Deprived /Average BME	11.8151	11.7945	0.0206
3. Average Deprivation /High BME	11.9967	11.9751	0.0215
4. Deprived /High BME	11.5218	11.5013	0.0205
5. Deprived /High Asian	10.5769	10.5610	0.0159

Comments

QALYs lived (discounted) in no intervention arm are lower for BME / more deprived cohorts

- 12.45 for England average, 10.56 for deprived/ high Asian

Intervention effect size makes a big difference to incremental QALYs e.g. England average

- 0.0012 (Intervention A), 0.0077 (Intervention C), 0.0261 (Intervention E)

For any intervention, QALYs gained are slightly smaller for more deprived / BME

- 0.0077 for England average (Intervention C)
- 0.0051 for deprived/ high Asian (Intervention C)

Table 22 Average Lifetime Discounted Costs of Healthcare Complications (i.e. Excluding Direct Public Health Intervention Costs) by Effect Size and by Cohort

INTERVENTION A: Very small BMI=-0.1 , SBP=-0.3, TC:HDL =.998	Intervention Costs of Healthcare (Discounted)	Control Costs of Healthcare (Discounted)	Costs of Healthcare Difference
1. England Average	£9,628	£9,631	-£3
2. Deprived /Average BME	£10,420	£10,423	-£3
3. Average Deprivation /High BME	£9,524	£9,532	-£8
4. Deprived /High BME	£10,444	£10,450	-£6
5. Deprived /High Asian	£11,002	£11,016	-£14
INTERVENTION B: Small effect BMI=-0. 3, SBP=-0.8, TC:HDL =.994			
1. England Average	£9,611	£9,631	-£20
2. Deprived /Average BME	£10,390	£10,423	-£33
3. Average Deprivation /High BME	£9,528	£9,532	-£4
4. Deprived /High BME	£10,448	£10,450	-£2
5. Deprived /High Asian	£11,004	£11,016	-£12
INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990			
1. England Average	£9,607	£9,631	-£24
2. Deprived /Average BME	£10,380	£10,423	-£43
3. Average Deprivation /High BME	£9,504	£9,532	-£28
4. Deprived /High BME	£10,415	£10,450	-£35
5. Deprived /High Asian	£10,976	£11,016	-£41
INTERV'N D:Substantial effect BMI=-1.0 , SBP=-2.7, TC:HDL =.980			
1. England Average	£9,564	£9,631	-£68
2. Deprived /Average BME	£10,327	£10,423	-£96
3. Average Deprivation /High BME	£9,476	£9,532	-£56
4. Deprived /High BME	£10,367	£10,450	-£83
5. Deprived /High Asian	£10,944	£11,016	-£72

INTERV'N E: Large effect BMI=-1.5 , SBP=-4.0, TC:HDL =.970			
1. England Average	£9,540	£9,631	-£91
2. Deprived /Average BME	£10,286	£10,423	-£137
3. Average Deprivation /High BME	£9,424	£9,532	-£109
4. Deprived /High BME	£10,317	£10,450	-£134
5. Deprived /High Asian	£10,908	£11,016	-£109

<u>Comments</u>

Healthcare costs (discounted) in no intervention arm are higher for BME / deprived cohorts

- £9,631 for England average, £11,016 deprived/ high Asian

The intervention effect makes a big difference to costs (-£= savings) e.g. England average

- £3 (Intervention A), - £24 (Intervention C), - £91 (Intervention E)

For any intervention, cost savings are slightly higher for more deprived / BME

- £24 for England average (Intervention C)
- £41 for deprived/ high Asian (Intervention C)

Table 23 Incremental Cost-Effectiveness by Effect Size and by Cohort Assuming Direct Public Health Intervention Package Cost (including follow-up) per participant of £100

INTERVENTION A: Very small BMI=-0.1 , SBP=-0.3, TC:HDL =.998	Incremental Costs (Discounted)	Incremental QALYs (Discounted)	Incremental Cost per QALY Gained
1. England Average	£94	0.0012	£78,127
2. Deprived /Average BME	£93	0.0011	£87,986
3. Average Deprivation /High BME	£89	0.0018	£50,618
4. Deprived /High BME	£90	0.0005	£178,185
5. Deprived /High Asian	£82	-0.0004	-£217,655 (not cost-effective and dominated)
INTERVENTION B: Small effect BMI=-0. 3, SBP=-0.8, TC:HDL =.994			
1. England Average	£76	0.0043	£17,910
2. Deprived /Average BME	£63	0.0037	£16,957
3. Average Deprivation /High BME	£92	0.0052	£17,877
4. Deprived /High BME	£95	0.0029	£32,304
5. Deprived /High Asian	£84	0.0024	£35,719
INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990			
1. England Average	£73	0.0077	£9,406
2. Deprived /Average BME	£54	0.0072	£7,415
3. Average Deprivation /High BME	£68	0.0084	£8,161
4. Deprived /High BME	£62	0.0051	£12,184
5. Deprived /High Asian	£56	0.0051	£11,025
INTERV'N D:Substantial effect BMI=-1.0 , SBP=-2.7, TC:HDL =.980			
1. England Average	£29	0.0172	£1,688
2. Deprived /Average BME	£0	0.0126	£37
3. Average Deprivation /High BME	£40	0.0153	£2,638
4. Deprived /High BME	£14	0.0141	£968
5. Deprived /High Asian	£24	0.0100	£2,423
INTERV'N E: Large effect BMI=-1.5 , SBP=-4.0, TC:HDL =.970			
1. England Average	£6	0.0261	£223
2. Deprived /Average BME	-£41	0.0206	-£1,980 Cost-effective and dominating
3. Average Deprivation /High BME	-£12	0.0215	-£553 Cost-effective and dominating
4. Deprived /High BME	-£37	0.0205	-£1,804 Cost-effective and dominating
5. Deprived /High Asian	-£12	0.0159	-£766

			Cost-effective and dominating

Comments

Intervention effect makes a big difference to cost per QALY for a £100 intervention

- e.g. For England average: £78,127 (intervention A), £9,406 (intervention C), £233 (intervention E)

For small to moderate interventions, the cost per QALY gained are 'worse' i.e. more cost to achieve the same effect in the more deprived / BME subgroups

- £9,406 for England average (Intervention C)
- £11,025 for deprived/ high Asian (Intervention C)

This is because the lower QALY gain achieved is not quite offset by the higher cost savings

Table 24 Incremental Cost-Effectiveness by Effect Size and by Cohort Assuming Direct Public Health Intervention Package Cost (including follow-up) per participant of £10

INTERVENTION A: Very small BMI=-0.1 , SBP=-0.3, TC:HDL =.998	Incremental Costs (Discounted)	Incremental QALYs (Discounted)	Incremental Cost per QALY Gained
1. England Average	£7	0.0012	£5,745
2. Deprived /Average BME	£6	0.0011	£6,086
3. Average Deprivation /High BME	£2	0.0018	£977
4. Deprived /High BME	£3	0.0005	£6,670
5. Deprived /High Asian	-£5	-0.0004	£12,096 **not** cost-effective
INTERVENTION B: Small effect BMI=-0. 3, SBP=-0.8, TC:HDL =.994			
1. England Average	-£11	0.0043	-£2,515 $^{\phi}$
2. Deprived /Average BME	-£24	0.0037	-£6,363 $^{\phi}$
3. Average Deprivation /High BME	£5	0.0052	£1,013 $^{\phi}$
4. Deprived /High BME	£8	0.0029	£2,650 $^{\phi}$
5. Deprived /High Asian	-£3	0.0024	-£1,174 $^{\phi}$
INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990			
1. England Average	-£14	0.0077	-£1,867 $^{\phi}$
2. Deprived /Average BME	-£33	0.0072	-£4,595 $^{\phi}$
3. Average Deprivation /High BME	-£19	0.0084	-£2,231 $^{\phi}$
4. Deprived /High BME	-£25	0.0051	-£4,963 $^{\phi}$
5. Deprived /High Asian	-£31	0.0051	-£6,098 $^{\phi}$
INTERV'N D:Substantial effect BMI=-1.0 , SBP=-2.7, TC:HDL =.980			
1. England Average	-£58	0.0172	-£3,363 $^{\phi}$
2. Deprived /Average BME	-£86	0.0126	-£6,886 $^{\phi}$

3. Average Deprivation /High BME	-£47	0.0153	-£3,057 $^{\phi}$
4. Deprived /High BME	-£73	0.0141	-£5,183 $^{\phi}$
5. Deprived /High Asian	-£63	0.0100	-£6,307 $^{\phi}$
INTERV'N E: Large effect BMI=-1.5 , SBP=-4.0, TC:HDL =.970			
1. England Average	-£81	0.0261	-£3,105 $^{\phi}$
2. Deprived /Average BME	-£128	0.0206	-£6,202 $^{\phi}$
3. Average Deprivation /High BME	-£99	0.0215	-£4,595 $^{\phi}$
4. Deprived /High BME	-£124	0.0205	-£6,040 $^{\phi}$
5. Deprived /High Asian	-£99	0.0159	-£6,244 $^{\phi}$

ϕ = Cost-effective and dominating

Table 25 Incremental Cost-Effectiveness by Effect Size and by Cohort Assuming Direct Public Health Intervention Package Cost (including follow-up) per participant of £1

INTERVENTION A: Very small BMI=-0.1 , SBP=-0.3, TC:HDL =.998	Incremental Costs (Discounted)	Incremental QALYs (Discounted)	Incremental Cost per QALY Gained
1. England Average	-£2	0.0012	-£1,493 $^{\phi}$
2. Deprived /Average BME	-£2	0.0011	-£2,104 $^{\phi}$
3. Average Deprivation /High BME	-£7	0.0018	-£3,987 $^{\phi}$
4. Deprived /High BME	-£5	0.0005	-£10,481 $^{\phi}$
5. Deprived /High Asian	-£13	-0.0004	£35,071 Cost-effective
INTERVENTION B: Small effect BMI=-0. 3, SBP=-0.8, TC:HDL =.994			
1. England Average	-£19	0.0043	-£4,558 $^{\phi}$
2. Deprived /Average BME	-£32	0.0037	-£8,695 $^{\phi}$
3. Average Deprivation /High BME	-£3	0.0052	-£674 $^{\phi}$
4. Deprived /High BME	-£1	0.0029	-£315 $^{\phi}$
5. Deprived /High Asian	-£11	0.0024	-£4,864 $^{\phi}$
INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990			
1. England Average	-£23	0.0077	-£2,994 $^{\phi}$
2. Deprived /Average BME	-£42	0.0072	-£5,796 $^{\phi}$
3. Average Deprivation /High BME	-£27	0.0084	-£3,270 $^{\phi}$
4. Deprived /High BME	-£34	0.0051	-£6,678 $^{\phi}$
5. Deprived /High Asian	-£40	0.0051	-£7,810 $^{\phi}$
INTERV'N D:Substantial effect BMI=-1.0 , SBP=-2.7, TC:HDL =.980			
1. England Average	-£67	0.0172	-£3,868 $^{\phi}$
2. Deprived /Average BME	-£95	0.0126	-£7,578 $^{\phi}$
3. Average Deprivation /High BME	-£55	0.0153	-£3,626 $^{\phi}$
4. Deprived /High BME	-£82	0.0141	-£5,798 $^{\phi}$
5. Deprived /High Asian	-£72	0.0100	-£7,180 $^{\phi}$
INTERV'N E: Large effect BMI=-1.5 , SBP=-4.0, TC:HDL =.970			
1. England Average	-£90	0.0261	-£3,437 $^{\phi}$
2. Deprived /Average BME	-£136	0.0206	-£6,624 $^{\phi}$
3. Average Deprivation /High BME	-£108	0.0215	-£5,000 $^{\phi}$
4. Deprived /High BME	-£133	0.0205	-£6,464 $^{\phi}$
5. Deprived /High Asian	-£108	0.0159	-£6,792 $^{\phi}$

ϕ = Cost-effective and dominating

Table 26 Incremental Cost-Effectiveness by Effect Size and by Cohort Assuming Direct Public Health Intervention Package Cost (including follow-up) per participant of £1000

INTERVENTION A: Very small BMI=-0.1 , SBP=-0.3, TC:HDL =.998	Incremental Costs (Discounted)	Incremental QALYs (Discounted)	Incremental Cost per QALY Gained
1. England Average	£963	0.0012	£801,947
2. Deprived /Average BME	£963	0.0011	£906,984
3. Average Deprivation /High BME	£958	0.0018	£547,029
4. Deprived /High BME	£960	0.0005	£1,893,328
5. Deprived /High Asian	£952	-0.0004	-£2,515,166 Not cost-effective and dominated
INTERVENTION B: Small effect BMI=-0. 3, SBP=-0.8, TC:HDL =.994			
1. England Average	£946	0.0043	£222,157
2. Deprived /Average BME	£933	0.0037	£250,158
3. Average Deprivation /High BME	£962	0.0052	£186,515
4. Deprived /High BME	£964	0.0029	£328,837
5. Deprived /High Asian	£954	0.0024	£404,655
INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990			
1. England Average	£942	0.0077	£122,132
2. Deprived /Average BME	£923	0.0072	£127,518
3. Average Deprivation /High BME	£938	0.0084	£112,080
4. Deprived /High BME	£931	0.0051	£183,652
5. Deprived /High Asian	£926	0.0051	£182,257
INTERV'N D:Substantial effect BMI=-1.0 , SBP=-2.7, TC:HDL =.980			
1. England Average	£899	0.0172	£52,194
2. Deprived /Average BME	£870	0.0126	£69,270
3. Average Deprivation /High BME	£910	0.0153	£59,585
4. Deprived /High BME	£883	0.0141	£62,477
5. Deprived /High Asian	£894	0.0100	£89,727
INTERV'N E: Large effect BMI=-1.5 , SBP=-4.0, TC:HDL =.970			
1. England Average	£875	0.0261	£33,495
2. Deprived /Average BME	£829	0.0206	£40,236
3. Average Deprivation /High BME	£858	0.0215	£39,873
4. Deprived /High BME	£833	0.0205	£40,554
5. Deprived /High Asian	£857	0.0159	£54,019

Comments on Table 24,

Table 25 and Table 26

The cost per QALY gained is 'worse', i.e. more cost to achieve the same effect, if direct intervention costs are higher e.g. England average (Intervention C). It is cost-saving for a direct intervention cost of £ 1 or £ 10 per person, cost-effective but not cost-saving for an intervention cost of £ 100 and not cost-effective for an intervention cost of £ 1000.

The cost of the intervention makes such a big difference to cost-effectiveness because –

- The intervention cost is a big driver of the lifetime effect on total costs (i.e. including healthcare costs)
- The incremental QALY gains per person are small in absolute terms

Table 27 Threshold Costs per participant for Public Health Intervention Package Cost (including follow-up) to be considered Cost-Effective at £20,000 per QALY

INTERVENTION A: Very small BMI=-0.1 , SBP=-0.3, TC:HDL =.998	Threshold Public Health Intervention Package Cost (including follow-up) to be considered Cost-Effective at £20,000 / QALY
1. England Average	£27
2. Deprived /Average BME	£24
3. Average Deprivation /High BME	£43
4. Deprived /High BME	£16
5. Deprived /High Asian	£7
INTERVENTION B: Small effect BMI=-0. 3, SBP=-0.8, TC:HDL =.994	
1. England Average	£106
2. Deprived /Average BME	£108
3. Average Deprivation /High BME	£108
4. Deprived /High BME	£61
5. Deprived /High Asian	£60
INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990	
1. England Average	£178
2. Deprived /Average BME	£188
3. Average Deprivation /High BME	£196
4. Deprived /High BME	£136
5. Deprived /High Asian	£142
INTERV'N D:Substantial effect BMI=-1.0 , SBP=-2.7, TC:HDL =.980	
1. England Average	£412
2. Deprived /Average BME	£347
3. Average Deprivation /High BME	£362
4. Deprived /High BME	£366
5. Deprived /High Asian	£272
INTERV'N E: Large effect BMI=-1.5 , SBP=-4.0, TC:HDL =.970	
1. England Average	£614
2. Deprived /Average BME	£549

3. Average Deprivation /High BME	£539
4. Deprived /High BME	£544
5. Deprived /High Asian	£426

Comments

The cost per QALY will depend on the direct costs of the initial intervention plus the cost of ongoing additional (over and above usual care) support necessary to help to sustain achieved effects.

The threshold for total package costs to be considered cost-effective depends upon

- the scale of effect size of the intervention
- the level of deprivation / BME in the cohort

Table 28 Sensitivity Analysis if Community Intervention Were Only Taken Up By People Who are Obese within the Cohort Assuming Direct Public Health Intervention Package Cost (including follow-up) per participant of £100

Intervention participants are those who are **obese only** (Zero uptake or cost associated with non-obese people within community)			
INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990	Incremental Costs (Discounted)	Incremental QALYs (Discounted)	Incremental Cost per QALY Gained
OB1. England Average	£8	0.0139	£587
OB2. Deprived /Average BME	-£5	0.0137	-£329 Cost-effective and dominating
OB3. Average Depriv'n /High BME	£15	0.0126	£1,222
OB4. Deprived /High BME	£8	0.0140	£554
OB5. Deprived /High Asian	£11	0.0115	£920
Intervention participants come from **all parts** of the community (for comparison)			
INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990	Incremental Costs (Discounted)	Incremental QALYs (Discounted)	Incremental Cost per QALY Gained
1. England Average	£73	0.0077	£9,406
2. Deprived /Average BME	£54	0.0072	£7,415
3. Average Deprivation /High BME	£68	0.0084	£8,161
4. Deprived /High BME	£62	0.0051	£12,184
5. Deprived /High Asian	£56	0.0051	£11,025

Comments

For an intervention of moderate effect size, targeting the obese has a large impact on both cost-effectiveness and the net impact on costs. The results suggest that targeting the obese would be a more cost-effective strategy than a strategy focussing on deprivation/BME alone

Table 29 and Table 30 below present results from sensitivity analyses with alternative assumptions for the effectiveness of the intervention on sustaining BMI and other risk factors below the level had there been no intervention. The alternative assumptions are that BMI returns to the level of the control arm in year 2 and year 7 respectively (compared to year 4 in the base case). Interventions C and B from the five what-if scenarios are used to illustrate the effect of these alternative regain assumptions.

Table 29 : Sensitivity Analysis if weight loss only maintained for the first year - Intervention C ; Direct Public Health Intervention Package Cost (including follow-up) per participant of £100

INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990	Incremental Costs (Discounted)	Incremental QALYs (Discounted)	Incremental Cost per QALY Gained
1. England Average	£77	0.0040	£19,365
2. Deprived /Average BME	£63	0.0041	£15,337
3. Average Deprivation /High BME	£86	0.0048	£17,810
4. Deprived /High BME	£92	0.0022	£42,400
5. Deprived /High Asian	£78	0.0022	£35,658
INTERVENTION B: Small effect BMI=-0. 3, SBP=-0.8, TC:HDL =.994	Incremental Costs (Discounted)	Incremental QALYs (Discounted)	Incremental Cost per QALY Gained
1. England Average	£83	0.0014	£57,637
2. Deprived /Average BME	£65	0.0028	£23,286

<u>Comments</u>

Assuming a cost per person of £ 100, If weight loss is regained immediately after the first year then the results suggest that the moderate effect scenario (Intervention C) is either just cost-effective or not cost-effective depending on which cohort is targeted.

Table 30 : Sensitivity Analysis if weight loss regained over a period of 6 years - Intervention C; Direct Public Health Intervention Package Cost (including follow-up) per participant of £100

INTERV'N C: Moderate effect BMI=-0. 5, SBP=-1.3, TC:HDL =.990	Incremental Costs (Discounted)	Incremental QALYs (Discounted)	Incremental Cost per QALY Gained
1. England Average	£67	0.0388	£1,719

2. Deprived /Average BME	£7	0.0354	£210
3. Average Deprivation /High BME	£40	0.0366	£1,089
4. Deprived /High BME	£24	0.0341	£709
5. Deprived /High Asian	£11	0.0309	£345

Comments

As expected, if weight loss could be partly sustained until then end of the 6th year at modest total cost per person of £ 100 over this duration, then the moderate intervention (C) would become very cost-effective (though not cost-saving).

4. DISCUSSION

Cost-effectiveness is, in most of our analyses, most strongly determined by -

- the Initial Intervention Cost
- the ongoing Support Costs
- the intervention Effect Size
- whether the Intervention is targeted at the whole population or obese only
- the durability of beneficial effects and
- to a lesser extent, by whether the intervention is targeted at the BME/deprived subgroups (versus the overall population)

4.1. Implications

Some of the intervention scenarios (1 and 5) did not demonstrate cost-effectiveness – this is because the estimated effects on markers of CVD risk and diabetes are not significant enough to result in a reduction in events.

The modelling suggests that Interventions 3 (broad dietary education/cooking skills), 6 (Multi-component – small scale intervention), and 9 (Large-scale, region-wide multi-component (like Hartslag Limburg) are cost-effective based on the mean reported effects. Intervention 9 appears to be not only highly cost-effective but also possibly cost-saving (depending on assumptions around cost of maintenance intervention), subject to the caveats described below Table 10.

Results in Table 29 highlight the need to achieve sustainable benefits (reduction in BMI etc) beyond just the first year in order for interventions to be cost-effective. As intensive individual-based NHS resources comparable to those available to intensive diabetes prevention trials are likely to be prohibitive (both from a cost and resource availability point of view), designing affordable but effective maintenance interventions beyond the first year will need to be a key consideration.

4.2. Limitations of the evidence base and modelling

Effectiveness data :

As already discussed, there is a large degree of uncertainty around the effectiveness of the interventions reported in smaller studies with small effect sizes. Results may not be the same when the intervention is replicated in clinical practice. Given this and that our modelling results are deterministic (uncertainty not included), caution is needed in interpreting the results for the 5 intervention scenarios.

Predictors of the reduction in cardiovascular events

BMI is an inferior predictor of cardiovascular risk compared to others measures such as waist-to-hip ratio that take account of the distribution of any excess weight. If interventions reduce BMI by primarily reducing abdominal fat then, existing BMI-driven CVD risk equations from observational data may underestimate the benefit of intervention. Conversely, intervention studies are needed to be able to show that reducing weight and BMI does actually reduce the risk of CVD.

Also, regular aerobic exercise can cause a reduction in both waist circumference and cardiometabolic risk, even without a change in BMI [22], so existing BMI-driven CVD risk equations will not predict the benefit of such interventions.

Similarly regarding risk of diabetes, in the Indian Diabetes Prevention Programme (IDPP) [23], in which patients were leaner at baseline compared to other large prevention trials such as the Finnish Diabetes Prevention Study [30] and the US Diabetes Prevention Programme [31], reduction in risk of diabetes was achieved in spite of lack of reduction in weight or waist circumference. UK migrant Asians may be different to the population in the IDPP but this is worth bearing in mind because our modelling is based on associations between BMI reduction and events. Potentially, some interventions may be beneficial for reduction in diabetes risk regardless of weight loss, an observation also suggested by the Finnish Diabetes prevention Study [25].

5. APPENDICES

Appendix 1 – Mapping review search strategies

The mapping review search strategies were used to search specific economic databases: NHS Economic Evaluation Database (via Wiley) and EconLit (via OVID SP).

Medline Search One Mapping Review

1 (prediabetes or pre?diabetes).ti,ab.

2 ((impaired glucose adj (level* or tolerance or regulation or metabolism)) or raised glucose tolerance or IGT or impaired fasting glucose or insulin resistance or metabolic syndrome or hyperinsulinaemia or non diabetic hyperglycaemia or abnormal blood glucose level* or dysglycaemia or intermediate hyperglycaemia).ti, ab.

3 (((type II or type 2) N1 diabetes) or T2D).tea.

4 1 or 2 or 3

5 *prediabetic state/ or *diabetes mellitus, type 2/

6 (risk* or prevent* or reduce* or protect* or limit* or control*).ti,ab.

7 *risk reduction behaviour/ or *risk factors/

8 ((prediabetes or pre?diabetes or ((impaired glucose adj (level* or tolerance or regulation or metabolism)) or raised glucose tolerance or IGT or impaired fasting glucose or insulin resistance or metabolic syndrome or hyperinsulinaemia or non diabetic hyperglycaemia or abnormal blood glucose level* or dysglycaemia or intermediate hyperglycaemia) or (((type II or type 2) adj diabetes) or T2D)) adj5 (risk* or prevent* or reduce* or protect* or limit* or control*)).ti,ab.

9 4 and 7

10 6 and 5

11 8 or 10 or 9

12 great britain/ or england/ or scotland/ or wales/ or northern ireland/

13 (uk or united kingdom or britain or gb or england or scotland or wales or northern ireland).ti,ab.

14 13 or 12

15 11 and 14

16 limit 15 to (english language and humans and yr="1990 -Current")

17 from 16 keep 1-912

Medline Search Two Mapping Review

1. (south asia* or black africa* or black caribbean* or pakistan* or bangladesh* or india* or (Ethnic adj1 minorit*)).ti,ab.

2. (blue collar or working class or underclass or low* class or low* income or poverty).ti,ab.

3. social* exclu*.ti,ab.

4. social* inclu*.ti,ab.

5. (depriv* or disadvantage* or inequalit* or underprivilege*).ti,ab.

6. *income/ or *poverty areas/ or *social class/ or *socioeconomic factors/

7. 1 or 2 or 3 or 4 or 5 or 6

8. *body mass index/ or *obesity/ or *food habits/

9. (obes* or waist circumference or BMI or nutrition or "bmi > 3?"or “bmi > 24” or diet or overweight).ti,ab.

10. (weight adj (gain or change or retention)).ti,ab.

11. *Motor Activity/ or *Exercise/

12. (physical* inactiv* or physical* activ* or physical exercise).ti,ab.

13. (sedentary lifestyle* or active lifestyle*).ti,ab.

14. *Physical exertion/ or *Physical fitness/

15. (blood pressure or cardiovascular disease or blood cholesterol).ti,ab.

16. (history adj5 diabet*).ti,ab.

17. gestational diabetes.ti,ab.

18. *Diabetes, gestational/ or *Genetic predisposition to disease/

19. (genetic* or hereditary).ti,ab.

20. (behaviour change or social marketing).ti,ab.

21. *social marketing/ or *health behaviour/ or *health knowledge, attitudes, practice/ or *health promotion/

22. (diabetes education or cultural sensitivity or culturally competent).ti,ab.

23. *cultural competency/ or *communication barriers/

24. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23

25. great britain/ or england/ or scotland/ or wales/ or northern ireland/

26. (UK or United Kingdom or Britain or GB or England or Scotland or Wales or Northern Ireland).ti,ab.

27. 25 or 26

28. 7 and 24 and 27

29. limit 28 to (english language and humans and yr="1990 -Current")

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