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Impact of Type 2 diabetes prevention programmes based on risk identification and lifestyle intervention intensity strategies: a cost-effectiveness analysis

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Abstract

Aim To develop a cost-effectiveness model to compare Type 2 diabetes prevention programmes that target different at-risk population subgroups through lifestyle interventions of varying intensity.

Methods An individual patient simulation model simulated the development of diabetes in a representative sample of adults without diabetes from the UK population. The model incorporates trajectories for HbA_{1c}, 2-h glucose, fasting plasma glucose, BMI, systolic blood pressure, total cholesterol and HDL cholesterol. In the model, patients can be diagnosed with diabetes, cardiovascular disease, microvascular complications of diabetes, cancer, osteoarthritis and depression, or can die. The model collects costs and utilities over a lifetime horizon. The perspective is the UK National Health Service and Personal Social Services. We used the model to evaluate the population-wide impact of targeting a lifestyle intervention of varying intensity to six population subgroups defined as at high risk for diabetes.

Results The intervention produces 0.0020 to 0.0026 incremental quality-adjusted life-years and saves £15 to £23 per person in the general population, depending on the subgroup targeted. Cost-effectiveness increases with intervention intensity. The most cost-effective options were to target South-Asian people and those with HbA_{1c} levels > 42 mmol/mol (6%).

Conclusion The model indicates that diabetes prevention interventions are likely to be cost-saving. The criteria for selecting at-risk individuals differentially has an impact on diabetes and cardiovascular disease outcomes, and on the timing of costs and benefits. The model is not currently able to account for potential differential uptake or efficacy between subgroups. These findings have implications for deciding who should be targeted for diabetes prevention interventions.

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Introduction

In the UK, there are 3.2 million people with diabetes [1]. The prevalence of diabetes is increasing with growing levels of obesity and an aging population. Lifestyle interventions targeted at those individuals known to be at higher risk of Type 2 diabetes have been shown to be effective in reducing its incidence [2]. There are many factors that influence an individual's risk of Type 2 diabetes including obesity, age, physical activity and a family history of Type 2 diabetes. People from certain communities and population groups are at higher risk, including people of South-Asian, African-Caribbean, black African and Chinese descent and those from lower socio-economic groups. Public health guidelines recommend lifestyle interventions for individuals at high risk of diabetes, and communities at high risk [3,4], and a national diabetes prevention programme is currently under development in England [5].

Interventions targeting alternative at-risk groups are considered to be cost-effective based on economic evaluations [3,4,6]; however, because of differences in the model structures used, it has not been possible to compare their relative cost-effectiveness. A recent review of economic

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What's new?

- We describe the first study to compare the cost-effectiveness of a lifestyle intervention, designed to prevent diabetes, across different high-risk population subgroups and different intervention intensities.
- We found that diabetes prevention programmes are potentially cost-saving over a lifetime horizon, regardless of risk criteria or intervention intensity.
- Our study estimates that a lifestyle intervention will have a differential impact on disease outcomes (diabetes vs. cardiovascular disease) and time horizon of cost savings in different high-risk groups.
- These findings should help policy-makers decide their objectives in developing suitable criteria for diabetes prevention programme content and eligibility.

evaluations for diabetes prevention interventions identified that, in order to compare prevention interventions within a common framework, it is necessary to incorporate multiple risk factors for diabetes, diabetes-related complications and obesity-related comorbidity outcomes [7].

The aim of the present study was to evaluate whether pragmatic diabetes prevention programmes of varying intensity have differential effects when targeted to alternative at-risk groups within the population through the use of a flexible new economic model.

Methods

School for Public Health Research diabetes prevention model

The School for Public Health Research (SPHR) diabetes model is a micro-simulation model with a lifetime horizon that was developed to forecast long-term health outcomes and healthcare costs for the evaluation of diabetes prevention strategies. The model was developed according to a new conceptual modelling framework to guide modellers when constructing complex public health models [8]. Given the complexity of this model, a detailed description of the methods and assumptions are provided in File S1 and the variables included can be found in File S2.

The model incorporates individual-level trajectories for BMI, HbA_{1c}, 2-h glucose, fasting plasma glucose, systolic blood pressure, total cholesterol and HDL cholesterol. The trajectories are based on statistical analysis of the Whitehall II cohort (File S1). The model was designed to simulate a representative sample of the UK population, by using individuals from survey data from the 2011 Health Survey for England [9]. Individuals aged < 16 years and those with a prior diagnosis of diabetes were excluded, leaving a population of 8038, from which individuals were sampled at random. The characteristics of this population and missing data imputation methods are described in File S1. Figure 1 shows the sequence of updating clinical characteristics and clinical events (see File S1 for a description). This sequence was repeated for every annual cycle of the model.

Detection of diabetes, hypertension and cardiovascular risk

In any model cycle, individuals with one or more visit to a general practitioner may receive an opportunistic diagnosis of diabetes, hypertension or statin eligibility. The trajectory for glycaemia, systolic blood pressure and cholesterol changes after treatment initiation. When an individual is diagnosed with Type 2 diabetes after two consecutive HbA_{1c} test results of > 47.5 mmol/mol (6.5%) the model simulates subsequent HbA_{1c} test results using the UK Prospective Diabetes Study (UKPDS) outcomes model [10]. Furthermore, if an individual is prescribed antihypertensive treatment or statins in line with national guidelines [11,12], their systolic blood pressure or total cholesterol is reduced in line with changes observed in randomized controlled trials [13,14] and held constant for all subsequent cycles. The frequency of visits to a general practitioner was estimated from data from the South Yorkshire cohort, adjusted for individual characteristics. Details of the study population and the method used to simulate general practice attendance are described in File S1.

Long-term health outcomes

The model simulates a number of health outcomes that are related to BMI and diabetes. Further details of how these conditions were diagnosed and all other health outcomes are provided in File S1. The QRISK2 algorithm was used to estimate the probability of a cardiovascular disease (CVD) event [15]. CVD events were allocated to either stable angina, unstable angina, myocardial infarction, transient ischaemic attack, stroke, death from coronary heart disease or vascular disease, according to probability distributions used in a previous Health Technology Assessment [16]. This source was also used to estimate subsequent CVD events if the first event was not fatal.

The probability of congestive heart failure was estimated using the Framingham Heart Study congestive heart disease risk model for men and women [17]. Microvascular events including renal failure, blindness, foot ulcer and amputation were simulated using the UKPDS outcomes models [10,18].

Breast and colorectal cancer incidence [19,20] was estimated from analysis of the EPIC-Norfolk cohort. The association between BMI and cancer was obtained from a large meta-analysis of prospective observational studies [21]. UK mortality statistics determined the risk of mortality after breast or colorectal cancer [22]. Osteoarthritis incidence and association with BMI and $HbA_{1c} \geq 48$ mmol/mol (6.5%)

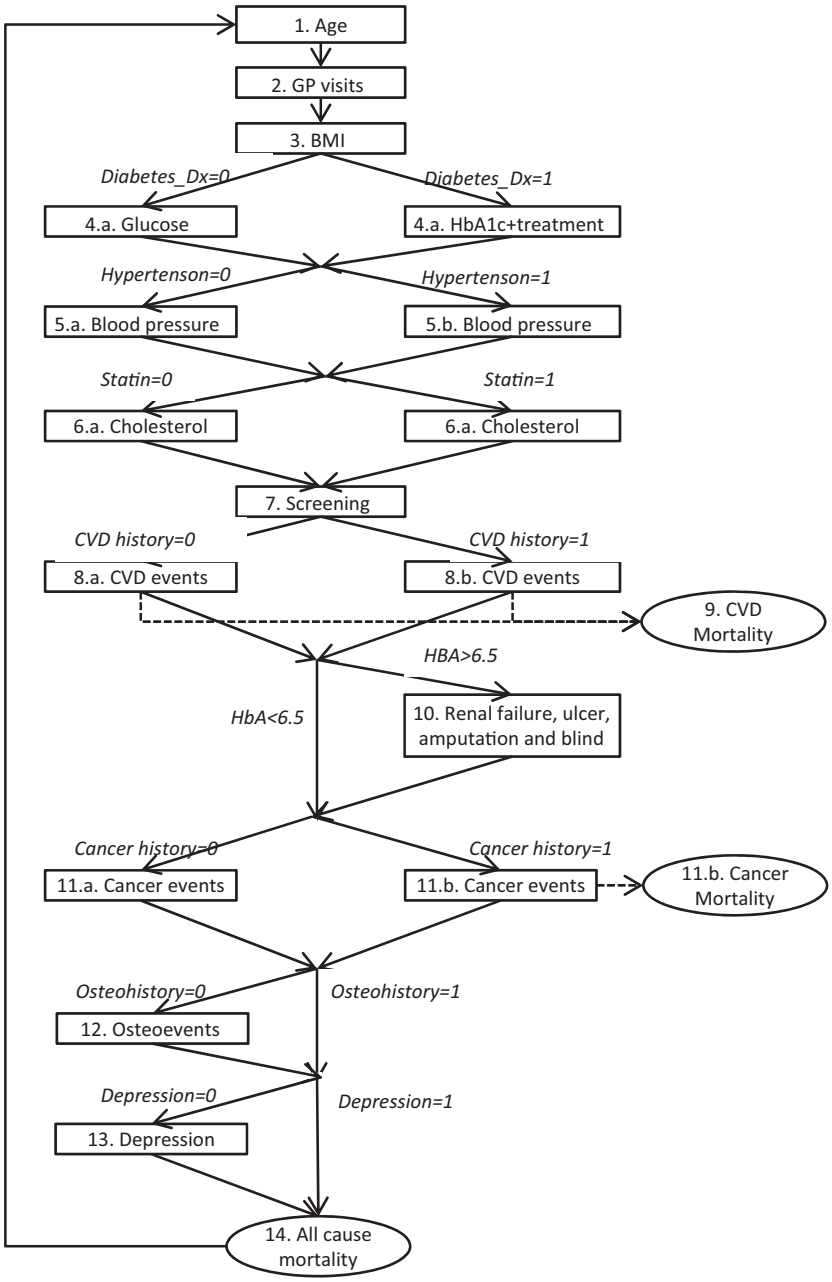

FIGURE 1 School for Public Health Research model schematic. Please see supplementary file 1 for a detailed description of the model schematic and how a hypothetical patient progresses through the model. CVD, cardiovascular disease; GP, general practice.

was estimated from analysis of an Italian observational cohort [23]. The incidence of depression in individuals without diabetes was obtained from a US cohort [24]. The risk of depression was inflated upon diagnosis of diabetes [24] and stroke [25].

Other-cause mortality describes the risk of death from any cause except CVD and cancer. Mortality rates by age and sex were extracted from the Office of National Statistics, excluding deaths from CVD, breast cancer, colorectal cancer and diabetes [26]. An increased risk of mortality was assigned to individuals with diabetes using data from a published meta-analysis [27].

Estimating costs and quality-adjusted life-years

Costs were estimated from a National Health Service and Personal Social Services perspective in 2012–2013 UK pounds sterling. Costs were assigned to the health outcomes simulated in the model to estimate an overall cost for each individual in the model.

At baseline, EQ-5D questionnaire scores were extracted from the Health Survey for England (HSE) dataset to describe an individual's health-related quality of life. A utility decrement for age was applied to the baseline EQ-5D score each year [16]. Change in BMI was also associated with a quality-of-life decrement [6]. CVD, cancer, microvascular disease osteoarthritis and depression were associated with a utility factor decrement which was multiplied by the individual's utility, adjusted for age and change in BMI. Costs and quality-adjusted life-years (QALYs) were discounted by 1.5% in line with the UK guidelines for public health interventions [28]. Details of how costs and utilities were estimated and how they were used in the model are given in File S1.

High-risk subgroups

We selected six sets of criteria to identify alternative subgroups of individuals at high risk of diabetes within the UK general population. The at-risk groups included individuals of South-Asian ethnicity, individuals in the lowest quintile of deprivation (low socio-economic status), individuals with HbA_{1c} > 42 mmol/mol (6%), individuals with BMI > 35 kg/m^2, individuals aged 40–65 years, and individuals with a Finnish Diabetes Risk (FINDRISC) 10 year probability score > 0.1 [29]. Summary characteristics for the six groups and the general population are reported in Table 1. To enable fair comparison between the six scenarios, we assumed that there was a budget constraint meaning that only 2% of the total adult population could be enrolled in the intervention.

Intervention

The effectiveness of the intervention was based on a recent meta-analysis of diabetes prevention programmes promoting dietary and/or physical activity lifestyle changes [2]. The review identified mean changes in BMI, HbA_{1c}, systolic blood pressure and total cholesterol. To make these changes conditional on baseline values, we estimated the percentage change over 12 months. The effects of the intervention were applied in the first year of the model to all enrolled individuals and were assumed to deteriorate over 5 years until the individual returned to their natural growth rate for metabolic risk factors, consistent with previous National Institute for Health and Care Excellence (NICE) evaluations [30].

The meta-analysis of diabetes prevention interventions [2] reported a gradient of effect on weight change and BMI according to adherence of the studies to prevention programme guidelines. We used this analysis to evaluate trade-offs between the investment in an intervention against its intensity (intensity is defined in broad terms of adherence to the guidelines). The default setting for our model was to evaluate a moderate intensity intervention, which was equivalent to the mean change in the meta-analysis. As alternative analyses, we examined the cost-effectiveness of low- and high-intensity interventions. The effectiveness data for these was based on assuming that either four fewer or four more NICE guidelines were followed during intervention implementation, given that adherence to NICE guidelines has been linked to increased weight loss at 12 months [2]. Direct effects on glycaemia, systolic blood pressure and total cholesterol were assumed to vary in line with the measured effects on BMI. The costs of low-, medium- and high-intensity interventions were an assumption based on intervention costs estimated in NICE public health guidance PH38 [30], and are shown in Table 2, together with effectiveness data.

Outcomes

We estimated the incremental costs and incremental QALYs generated by the intervention compared with the 'do-nothing' control, averaged across the whole adult general population simulated, rather than just the inter-

Table 1 Summary of subpopulation characteristics

	General UK population	Age 40–65 years	Low socio-economic status	HbA_{1c} > 42 mmol/mol (6%)	Finnish Diabetes Risk probability score > 0.1	BMI ≥ 35 kg/m^2	South-Asian
Total population, %	100	48	18	15	12	8	4
Male, %	44	44	44	45	40	34	42
White, %	90	92	80	92	96	91	0
Low socio-economic status, %	18	15	100	16	16	24	37
Mean (SD) age	48.6 (18.4)	54.1 (8.4)	44.7 (8.2)	61.2 (16.0)	66.3 (14.0)	50.0 (16.0)	38.3 (13.6)
Mean (SD) BMI, kg/m^2	27.2 (5.4)	27.9 (5.3)	27.4 (5.9)	28.7 (5.5)	34.21 (4.0)	39.0 (4.0)	26.6 (5.3)
Mean (SD) HbA_{1c}, mmol/mol	38	39	38	44	41	39	32
Mean (SD) HbA_{1c}, %	5.6 (0.5)	5.7 (0.4)	5.6 (0.5)	6.2 (0.1)	5.9 (0.5)	5.7 (0.6)	5.1 (0.5)
Mean (SD) systolic blood pressure, mmHg	125 (17.1)	128 (16.5)	125 (17.0)	133 (17.3)	135 (17.0)	128 (16.9)	120 (15.5)
Mean (SD) total cholesterol, mmol/l	5.4 (1.1)	5.7 (1.0)	5.3 (1.1)	5.8 (1.0)	5.8 (1.0)	5.5 (1.0)	5.2 (1.1)
Mean (SD) HDL cholesterol, mmol/l	1.5 (0.4)	1.6 (0.5)	1.5 (0.4)	1.5 (0.5)	1.5 (0.4)	1.5 (0.4)	1.4 (0.4)

Table 2 Effectiveness of hypothetical prevention intervention

	Low intensity	Medium intensity	High intensity
% change in BMI from baseline	−1.3	−3.0	−4.7
% change in Hba1c from baseline	−1.0	−2.2	−3.4
% change in systolic blood pressure from baseline	−1.9	−4.3%	−6.7
% change in total cholesterol from baseline	−1.5	−3.4	−5.3
Intervention cost	£43	£100	£157
Follow-up cost	£26	£60	£94

vention beneficiaries. As the intervention was cost-saving in every analysis, incremental cost-effectiveness ratios were negative. To overcome the problems with ranking negative incremental cost-effectiveness ratios, we estimated the overall incremental monetary benefit of the interventions per person by assuming a willingness to pay (λ) of £20,000 per QALY. Net benefit values above zero are cost-effective, with higher values being more cost-effective than lower values.

$$\text{incremental net benefit} = \lambda(\text{incremental QALY}) - (\text{incremental cost})$$

The model also allowed us to estimate the incremental change in diabetes and CVD diagnoses. Outcomes were collected after 1 year, 5 years, 10 years and lifetime to estimate the timings of cost-savings. To investigate parameter uncertainty, 1000 probabilistic sensitivity analysis samples were run for a total population of 20 000 individuals for the default moderate intensity intervention targeting all population subgroups (File S3). Deterministic analysis using one million individuals was used to obtain results for all three intervention intensities, together with a series of one-way sensitivity analyses. A full list of sensitivity analyses/assumptions tested is reported in File S4.

Results

The estimated incremental cost-effectiveness results for the deterministic analysis are reported in Table 3. All three intervention intensities increase QALYs and are cost-saving over the lifetime of the population, compared with doing nothing. High-intensity interventions are more cost-effective than interventions of moderate or low intensity.

Table 3 Incremental simulated outcomes for one million individuals in the general population (adult 16-99) over a lifetime perspective

	Targeting strategy					
	Adults aged 40–65 years	Low socio-economic status	HbA_{1c} > 42 mmol/mol (6%)	Finnish Diabetes Risk probability score > 0.1	BMI > 35 kg/m^2	South-Asian
A: Incremental net benefit (per person)						
Low intensity	£29	£32	£35	£26	£31	£31
Medium intensity	£62	£73	£74	£55	£66	£74
High intensity	£92	£103	£107	£80	£101	£108
B: Incremental total discounted costs (per person)						
Low intensity	−£8	−£9	−£12	−£7	−£13	−£9
Medium intensity	−£17	−£21	−£23	−£15	−£23	−£22
High intensity	−£23	−£30	−£34	−£20	−£36	−£32
C: Incremental total discounted QALYs (per person)						
Low intensity	0.0010	0.0012	0.0011	0.0010	0.0009	0.0011
Medium intensity	0.0022	0.0026	0.0025	0.0020	0.0021	0.0026
High intensity	0.0034	0.0037	0.0036	0.0030	0.0033	0.0038
D: Incremental life-years						
Low intensity	1658	1912	1562	1659	1687	1796
Medium intensity	3417	4546	3683	3468	3875	4456
High intensity	5329	6716	5560	5007	5901	6445
E: Incremental cost-effectiveness ratios (£ per QALY)						
Low intensity	−£8,388	−£7,694	−£10,823	−£7,646	−£13,948	−£8,217
Medium intensity	−£7,692	−£8,230	−£9,136	−£7,143	−£10,803	−£8,385
High intensity	−£6,761	−£8,026	−£9,281	−£6,806	−£10,954	−£8,274
F: Incremental diabetes diagnosis						
Low intensity	−37	−36	−111	−100	−49	1
Medium intensity	−97	−62	−229	−201	−127	5
High intensity	−121	−83	−336	−304	−197	−15
G: Incremental cardiovascular disease events						
Low intensity	−217	−223	−220	−190	−238	−188
Medium intensity	−497	−493	−457	−421	−519	−478
High intensity	−756	−736	−676	−641	−754	−716

QALY, quality-adjusted life-years.

Comparisons between subgroups indicate large variations in lifetime costs, QALYs and net benefits accrue for different subpopulations. Targeting interventions to South-Asian people, individuals with HbA_{1c} > 42 mmol/mol (6%) or individuals from low socio-economic backgrounds are the most cost-effective options. Targeting individuals with a high FINDRISC score is less cost-effective than any other option.

Table 4 reports the incremental costs at 1 year, 5 years and 10 years to describe how the initial intervention investment is reduced over time as a result of cost savings. Interventions for individuals identified by FINDRISC probability score > 0.1 or HbA_{1c} > 42 mmol/mol (6%) have the greatest cost savings after 1–10 years. Low socio-economic status and South-Asian groups take longer to recover costs despite generating high lifetime cost savings. This show that the interventions which are most likely to accrue the highest net benefit over a lifetime are not necessarily the most cost-saving in the short term.

There are important differences between the subgroups in how health benefits are distributed in terms of disease events. Interventions in adults aged 40–65 years, South-Asians and those with low socio-economic status have a large impact in reducing CVD, but have less effect, if any, in reducing lifetime diabetes. By contrast, intervening in individuals identified by a FINDRISC probability score > 0.1 or HbA_{1c} > 42 mmol/mol (6%) has a large impact in reducing diabetes diagnosis, but is slightly less effective in reducing CVD events.

Results from the probabilistic sensitivity analyses indicate that the intervention is highly likely to save costs and gain QALYs in all six subgroups, as the vast majority of probabilistic sensitivity analysis results are located in the south-east quadrant of the cost-effectiveness plane (Fig. 2 and File S3). Probabilistic sensitivity analysis results differ slightly from deterministic results because of the non-linearity of the model. Cost-effectiveness acceptability curves indicate that no individual subgroup has a particularly high probability of using resources most cost-effectively, but that the intervention is very unlikely to be more cost-effective to implement in individuals with a high FINDRISC score than in other subgroups (Fig. 2). Uncertainty around the cost-effectiveness of alternative subgroups is stable over different willingness-to-pay thresholds.

Finally, the intervention remains cost-effective in all population subgroups in all deterministic sensitivity analyses, and in most cases the South-Asian or HbA_{1c} > 42 mmol/mol (6%) subgroups remain the most cost-effective. A detailed description of the results from the sensitivity analysis can be found in File S4.

Table 4 Incremental cost (£ per person) after 1 year, 5 years and 10 years

	Adults aged 40–65 years			Low socio-economic status			HbA_{1c} > 42 mmol/mol (6%)			Finnish Diabetes Risk probability score > 0.1			BMI > 35 kg/m^2			South-Asian		
Year	1	5	10	1	5	10	1	5	10	1	5	10	1	5	10	1	5	10
Low intensity	0.79	1.39	−0.31	0.79	1.49	0.10	0.77	0.91	−1.82	0.68	0.64	−1.72	0.75	1.14	−0.74	0.82	1.83	0.85
Medium Intensity	1.84	3.62	0.24	1.85	3.71	0.95	1.76	2.46	−3.21	1.66	1.98	−2.96	1.79	3.06	−0.62	1.88	4.35	2.41
High Intensity	2.89	5.93	1.01	2.93	6.23	2.29	2.82	4.38	−3.70	2.66	3.70	−3.39	2.84	5.22	−0.07	2.99	6.99	4.22

Discussion

The analysis has shown that there are potentially substantial gains in health and cost savings available from diabetes prevention interventions, regardless of population target or

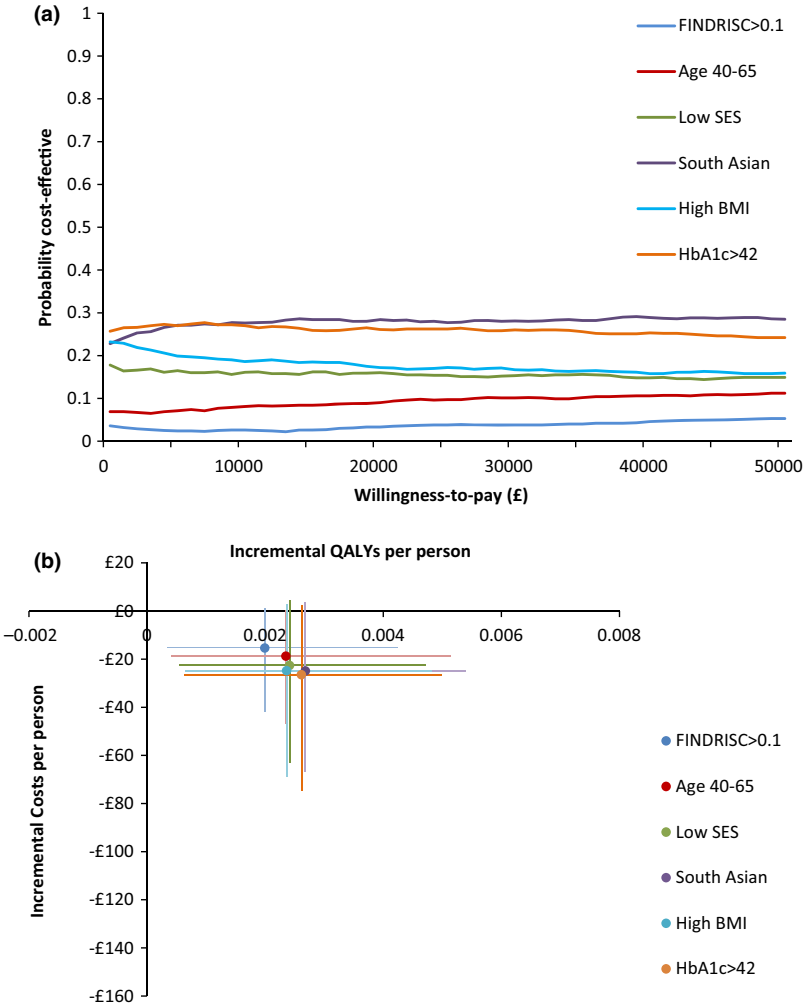

FIGURE 2 (a) Cost-effectiveness acceptability curve comparing the probability of cost-effectiveness of the moderate intensity intervention in six population subgroups. (b) Location on the cost-effectiveness plane of the mean incremental probabilistic sensitivity analyses results for the moderate intensity intervention compared with the 'do nothing' control in each of the six population subgroups. Crosses represent 95% CIs for costs and quality-adjusted life-years. FINDRISC, Finnish Diabetes Risk; SES, socio-economic status.

intensity. The new SPHR diabetes prevention model was developed so that diabetes prevention interventions with different weight change outcomes can be flexibly specified to target alternative populations reflecting multiple risk factors for diabetes and CVD. The analysis highlights that population heterogeneity will affect the cost-effectiveness of public health interventions. We found that applying the same intervention in different high-risk groups produces very different cost savings and QALY gains, events avoided and timings for the cost savings.

Targeting South-Asian populations generates the greatest overall lifetime net benefit because of the importance of preventing CVD, but actually increases the lifetime incidence of Type 2 diabetes. This counterintuitive result can be explained by individuals surviving CVD and living longer, thereby having more time to develop diabetes later in life. Cost savings are slow to accrue in this group (as in the group with low socio-economic status) because of the relative youth of individuals at the model start. Conversely, an HbA_{1c} concentration > 42 mmol/mol (6%) and a FINDRISC probability score > 0.1 are the most effective subgroups to target to reduce diabetes diagnoses, and generate the greatest short-term cost savings, although targeting individuals with HbA_{1c} > 42 mmol/mol (6%) is a much more cost-effective strategy than targeting those with FINDRISC probability score > 0.1.

The analysis described in the present paper is limited by an absence of evidence. In particular, we were not able to obtain estimates of how intervention effect sizes or intervention costs might vary by subgroup (e.g. through ease of recruitment), which limits our ability to make recommendations about which individuals should be targeted. Further research involving subgroup analysis would be extremely useful to inform this variable. More generally, the analysis assumed that the reduction in metabolic trajectories after intervention was proportionate to the individual's baseline values;

however, in reality, individuals will vary hugely in their response to intervention, and individuals with very low risk factors may not experience the same proportionate reduction. Finally, we based the model on diagnosis of individuals through HbA_{1c}, but other diagnostic methods (e.g. fasting plasma glucose) will identify a different subset of individuals with diabetes [31]; however, we think this is unlikely to significantly alter the results at the population level.

Two previous UK-based economic evaluations have found lifestyle interventions for diabetes prevention are cost-effective but not cost-saving in subgroups with either low socioeconomic status or high diabetes risk score and HbA_{1c} > 42 mmol/mol (6%) [3,4]. There are a number of factors that we believe can explain the differences. Firstly, the SPHR model includes a broader range of health outcomes such as depression, osteoarthritis, breast and colorectal cancer that were not included in previous evaluations. Secondly, the costs of major events, such as cardiovascular disease have increased as a result of inflation. Thirdly, the cost of screening individuals for Type 2 diabetes in order to identify individuals at high risk because of hyperglycaemia was not included in the SPHR model.

In the present analysis, we investigated six high risk groups separately, but it is highly likely that combining criteria could optimize resource allocation to a subpopulation with even greater gains in health and cost savings. The SPHR model can be easily modified to evaluate combined treatment criteria, in addition to a variety of alternative policies for Type 2 diabetes prevention. UK policy-makers can use this model to decide which populations they wish to target with lifestyle interventions according to their overall objectives, whether short- or long-term gains, equity or efficiency, or preventing CVD or diabetes.

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Competing interests

None declared.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

File S1 Supplementary methods.
File S2 Table of model variable, distributions and data sources.
File S3 Supplementary results.
File S4 Deterministic sensitivity analyses.