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The 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

Aims To develop a cost-effectiveness model to compare Type 2 diabetes prevention programmes targeting different at-risk population subgroups with a lifestyle intervention of varying intensity.

Methods An individual patient simulation model was constructed to simulate 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. 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 high risk for diabetes.

Results The intervention produces 0.0003 to 0.0009 incremental quality-adjusted life years and saves up to £1.04 per person in the general population, depending upon the subgroup targeted. Cost-effectiveness increases with intervention intensity. The most cost-effective options are to target individuals with HbA_{1c} > 42 mmol/mol (6%) or with a high Finnish Diabetes Risk (FINDRISC) probability score (> 0.1).

Conclusion The model indicates that diabetes prevention interventions are likely to be cost-effective and may be cost-saving over a lifetime. In the model, the criteria for selecting at-risk individuals differentially impact upon diabetes and cardiovascular disease outcomes, and on the timing of benefits. These findings have implications for deciding who should be targeted for diabetes prevention interventions.

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Introduction

In the United Kingdom (UK), there are 3.5 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]. Many factors influence an individual's risk of Type 2 diabetes including obesity, age, physical activity and a family history of the disease. 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 and communities at high risk of diabetes [3,4], and a national diabetes prevention programme is currently under development in England [5].

Interventions targeting alternative at-risk groups are considered 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 evaluations for

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What's new?

- We describe the first study to compare the cost-effectiveness of a lifestyle intervention to prevent diabetes across different high-risk population sub-groups and over different intervention intensities.
- We find that diabetes prevention programmes are cost-effective 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 the time horizon of cost savings in different high-risk groups.
- These findings should help policymakers decide their objectives in developing suitable criteria for diabetes prevention programme content and eligibility.

diabetes prevention interventions identified that 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].

This article aims to evaluate whether pragmatic diabetes prevention programmes of varying intensity have differential effects when targeted at alternative at-risk groups within the population through the use of a flexible new economic model.

Methods

The School for Public Health Research diabetes prevention model

The School for Public Health (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 in accordance with 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 Supporting Information File S1 and parameter values can be found in Supporting Information 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 upon statistical analysis of the Whitehall II cohort [9]. 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 [10]. 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 Supporting Information File S1. Figure 1 illustrates the sequence of updating clinical characteristics and clinical events (see Supporting Information File S1). 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 general practitioner (GP) visits may receive an opportunistic diagnosis of diabetes, hypertension or statin eligibility. The Whitehall II trajectory model determines HbA_{1c}, systolic blood pressure and cholesterol test results. Following diagnosis and treatment initiation, the trajectories for these risk factors are modified. When an individual is diagnosed with Type 2 diabetes following two consecutive HbA_{1c} tests > 47.5 mmol/mol (6.5%), the model simulates subsequent HbA_{1c} test results using the UK Prospective Diabetes Study (UKPDS) outcomes model [11]. Furthermore, if an individual is prescribed anti-hypertensive treatment or statins in line with national guidelines [12,13], their systolic blood pressure or total cholesterol is reduced in line with changes observed in randomized controlled trials [14,15] and held constant for all subsequent cycles. The frequency of GP visits was estimated from data from the South Yorkshire cohort adjusted for individual characteristics. Details of the study population and the method to simulate GP attendance are described in Supporting Information File S1.

Long-term health outcomes

The model simulates several 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 QRISK®2 algorithm was used to estimate the probability of a cardiovascular disease (CVD) event conditional on metabolic data, smoking, ethnicity, deprivation, diabetes and other covariates included in the equation [16].

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 [17]. 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 from the Framingham Heart Study congestive heart disease risk model for men and women [18]. Microvascular events including renal failure, blindness, foot ulcer and amputation were simulated using the UKPDS outcomes models [11,19].

Breast and colorectal cancer incidence [20,21] was estimated from analysis of the EPIC-Norfolk cohort. The

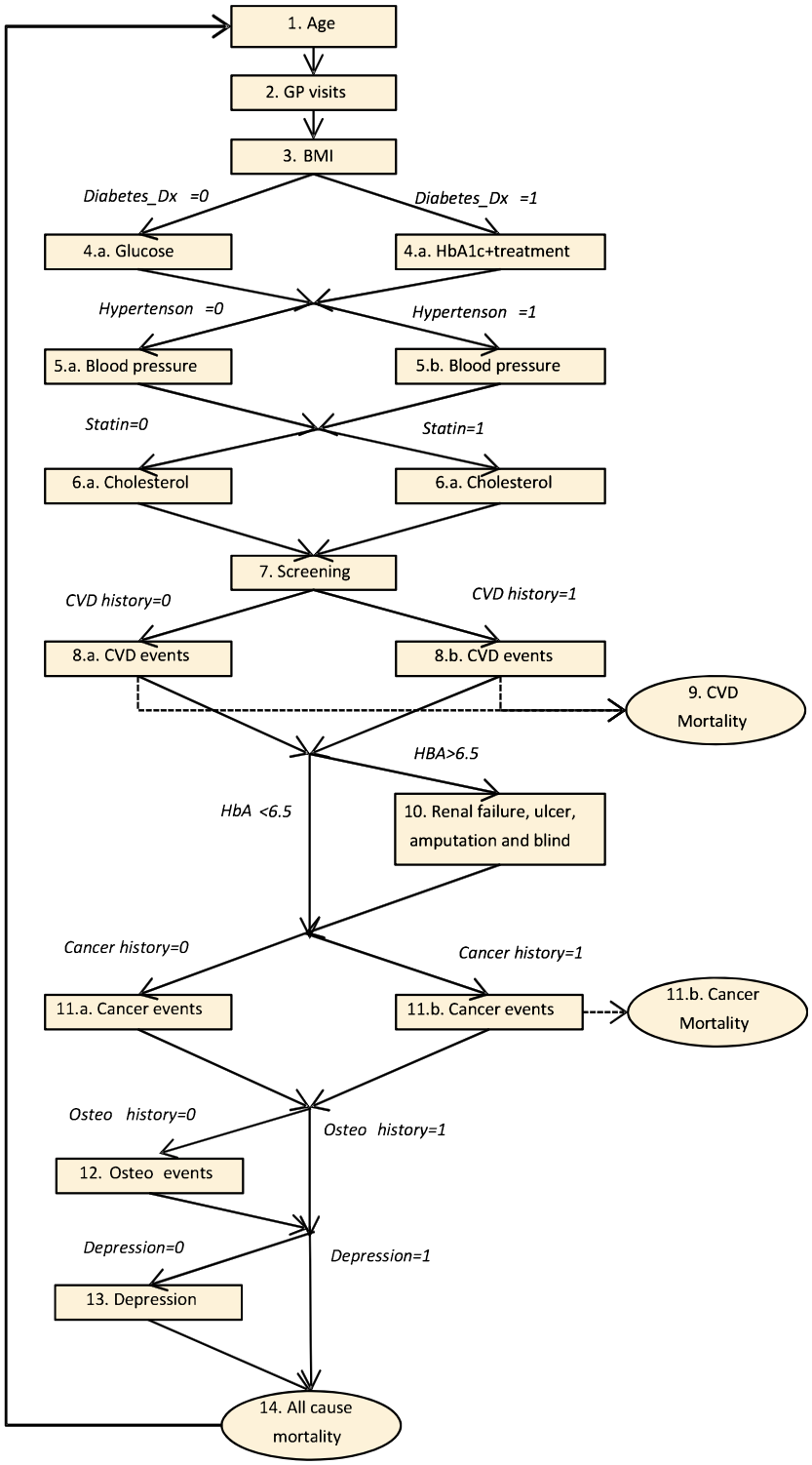

FIGURE 1 SPHR model schematic. See Supporting Information File S1 for a detailed description of the model schematic and how a hypothetical patient progresses through the model.

association between BMI and cancer was obtained from a large meta-analysis of prospective observational studies [22]. UK mortality statistics determined the risk of mortality after breast or colorectal cancer [23]. Osteoarthritis incidence and association with BMI and $HbA_{1c} \geq 48$ mmol/mol (6.5%) were estimated from analysis of an Italian observational cohort [24]. The incidence of depression in individuals without diabetes was obtained from a United States cohort

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 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
Age, years (SD)	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)
BMI, kg/m^2 (SD)	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)
HbA_{1c}, mmol/mol (SD)	38	39	38	44	41	39	32
HbA_{1c}, % (SD)	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)
Systolic blood pressure, mmHg (SD)	125 (17.1)	128 (16.5)	125 (17.0)	133 (17.3)	135 (17.0)	128 (16.9)	120 (15.5)
Total cholesterol mmol/l (SD)	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)
HDL cholesterol, mmol/l (SD)	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)

[25]. The risk of depression was inflated upon diagnosis of diabetes [25] and stroke [26].

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 for National Statistics, excluding deaths due to CVD, breast cancer, colorectal cancer and diabetes [27]. An increased risk of mortality was assigned to individuals with diabetes using data from a published meta-analysis [28].

Estimating costs and quality-adjusted life-years

Costs were estimated from a National Health Service (NHS) and personal social services perspective in 2014–2015 UK pounds (£). 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 scores were extracted from the Health Survey for England dataset to describe an individual's health-related quality of life. A utility decrement for age was applied to the baseline EQ-5D each year [17]. 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. Costs and quality-adjusted life-years (QALYs) were discounted by 1.5% in line with the UK guidelines for public health interventions [29]. Details of how costs and utilities were estimated and how they were used in the model are detailed in Supporting Information File S1.

The 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, and individuals with a Finnish Diabetes Risk (FINDRISC) probability score > 0.1 [30]. Summary characteristics for the six groups and the general population are reported in Table 1. The proportion of individuals meeting each of the criteria is reported in Table 1. This shows that some subgroups (age 40–65) describe a much larger proportion of the population than others (South Asian). 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, regardless of the size of the subgroup. This means that in some groups there will be more under-utilization of the intervention than other.

The 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 and Excellence (NICE) evaluations [31].

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 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 upon an assumption 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. An adjustment was made to the metabolic growth models to avoid double counting of the indirect effects of BMI on other metabolic risk factors. The costs of low-, medium- and high-intensity interventions were an assumption based on intervention costs estimated in NICE public health guidance PH38 [31], and are presented in Table 2 together with effectiveness data. An additional cost of an HbA_{1c} test (£3) was added to the HbA_{1c} group to account for the additional cost of identifying these patients assuming approximately seven people would need to be screened to identify one participant.

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 intervention beneficiaries. Because the intervention was cost saving some incremental cost-effectiveness ratios were negative, implying the intervention dominates do nothing. 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.

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 (year 1)	£43	£100	£157
Follow-up cost per year (years 2–4)	£26	£60	£94

$$\text{inc.Net Benefit} = \lambda(\text{inc.QALY}) - (\text{inc.COST})$$

The model also allowed us to estimate the incremental change in diabetes and CVD diagnoses. Outcomes were collected after up to 15 years and lifetime to estimate the timings of cost-savings. To investigate parameter uncertainty, 2000 probabilistic sensitivity analyses samples were run for 20 000 randomly selected individuals per run for the high-intensity intervention targeting all population subgroups (Supporting Information 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 Supporting Information File S4.

Results

The deterministic incremental cost-effectiveness results for the adult general population are reported in Table 3. The results describe the net benefit, incremental costs and incremental QALYs averaged across the whole adult population. All three intervention intensities increase QALYs and are cost-effective over the lifetime of the population, compared with doing nothing. High-intensity interventions are more cost-effective than interventions of moderate- or low-intensity. Comparisons between subgroups indicate large variations in lifetime costs, QALYs and net benefits accrued for different subpopulations. Targeting interventions to individuals with $HbA_{1c} > 42$ mmol/mol (6%), individuals with high FINDRISC probability score (> 0.1) or individuals with high BMI are the most cost-effective options. Targeting South Asian individuals is less cost-effective than any other option. The incremental results for the individuals receiving the intervention are reported in Supporting Information File S3.

Figure 2 illustrates the incremental costs at over 15 years post intervention to describe how the initial intervention investment is reduced over time due to cost savings. Interventions for individuals identified by FINDRISC > 0.1 or $HbA_{1c} > 42$ mmol/mol (6%) have the smallest costs over 15 years. Low socio-economic status and South Asian groups take longer to recover costs and are not cost-saving over a lifetime. There are important differences between the subgroups in how health benefits are distributed in terms of disease events. Interventions in adults aged 40–65, South Asians and low socio-economic status groups have a similar reduction in both CVD and diabetes cases. By contrast, intervening in individuals identified with the FINDRISC > 0.1 or $HbA_{1c} > 42$ mmol/mol (6%) has a disproportionately large impact in reducing diabetes diagnosis compared with other subgroups, but is only marginally more effective in reducing CVD events.

Results from the probabilistic sensitivity analyses indicate that the intervention is a likely gain of QALYs in all six

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

Absolute values	Intensity	Targeting strategy (incremental results vs. do nothing)					
Do nothing		Adults aged 40–65	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	2.80	2.38	9.63	6.29	5.15	1.40
	Medium	6.26	4.93	18.93	14.43	10.04	3.96
	High	9.72	6.85	27.15	22.44	14.41	5.70
	B: Incremental total discounted costs per person (£)						
£36 373	Low	0.36	0.76	−0.71	−0.36	−0.84	1.15
	Medium	1.58	2.10	−0.99	−1.04	−0.24	2.86
	High	2.28	2.77	−2.47	−1.39	−0.24	4.28
	C: Incremental total discounted QALYs (per person)						
15.548	Low	0.00016	0.00045	0.00030	0.00030	0.00022	0.00013
	Medium	0.00039	0.00090	0.00067	0.00067	0.00049	0.00034
	High	0.00060	0.000123	0.00123	0.00105	0.00073	0.00050
	D: Incremental life years						
32.25 million*	Low	217	125	687	407	197	108
	Medium	580	468	1444	1010	635	372
	High	757	577	1816	1621	978	496
	E: ICERs (£ per QALY)						
	Low	2263	4,839	Dominates	Dominates	Dominates	9027
	Medium	4,024	5967	Dominates	Dominates	Dominates	8381
	High	3,808	5759	Dominates	Dominates	332	8581
	E: Incremental diabetes diagnosis						
550 000*	Low	−19	−17	−83	−63	−20	−3
	Medium	−29	−32	−161	−121	−38	−1
	High	−38	−51	−235	−176	−71	−4
	F: Incremental cardiovascular disease events						
480 000*	Low	−8	−12	−16	−15	−15	−2
	Medium	−30	−22	−33	−40	−20	−3
	High	−40	−33	−50	−69	−31	−14

*Rounded to nearest ten thousand. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

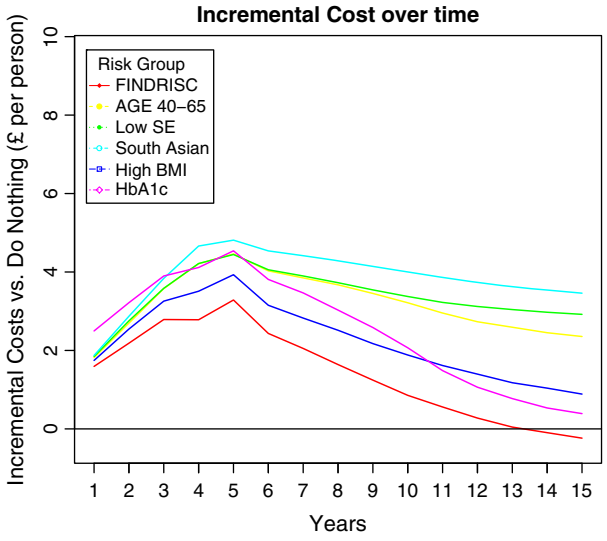

FIGURE 2 Incremental cost (£ per person in the general population) over 15 years. FINDRISC, Finnish Diabetes Risk; SE, socio-economic status.

subgroups, because the vast majority of probabilistic sensitivity analyses results are located in the southeast or northeast quadrants of the cost-effectiveness plane (Fig. 3 and Supporting Information File S3). The intervention is also highly likely to be cost-effective in all subgroups at a threshold of £20 000/QALY, because probabilistic sensitivity analyses results are predominantly located to the right of the cost-effectiveness threshold (dotted line in Fig. 3b). Probabilistic sensitivity analyses results differ slightly from deterministic results due to the non-linearity of the model. The cost-effectiveness acceptability curve indicates that the HbA_{1c} > 42 mmol/mol (6%) group has a high probability of cost-effectiveness compared with do nothing (Fig. 3b). Uncertainty around the cost-effectiveness of HbA_{1c} > 42 mmol/mol (6%) 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 all cases the HbA_{1c} > 42 mmol/mol (6%) subgroup remains the most cost-effective. A detailed description of the results from the sensitivity analysis can be found in Supporting Information File S4.

Discussion

The analysis has shown that there are potentially substantial gains in health and cost savings available from diabetes prevention interventions depending upon the population

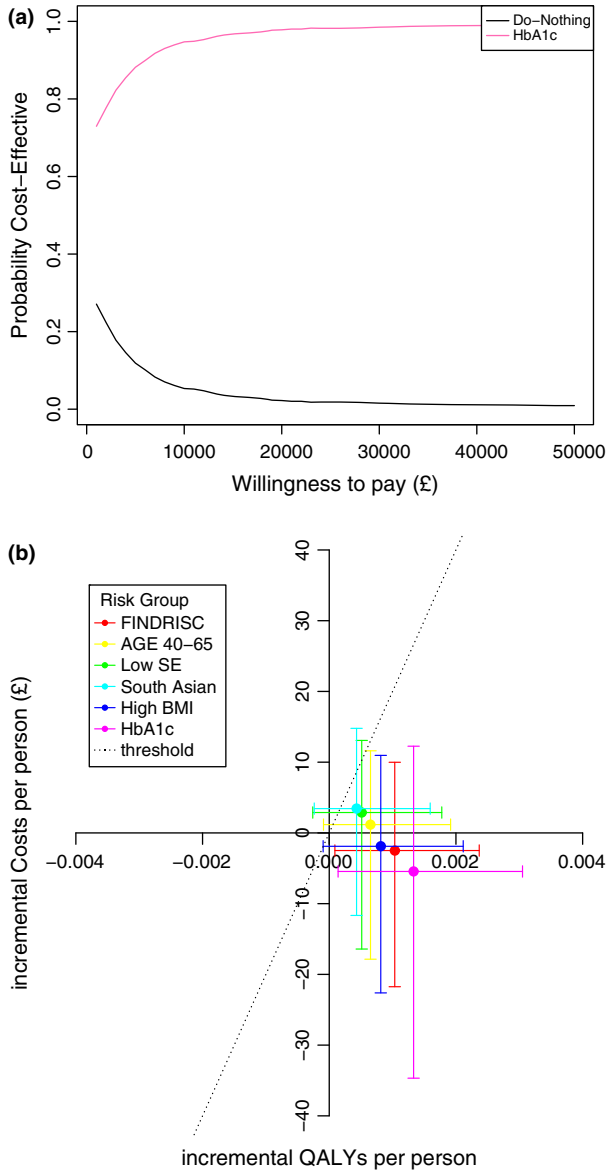

FIGURE 3 (a) Cost-effectiveness acceptability curve comparing the probability cost-effective of the moderate intensity intervention in six population subgroups. (b) Location on the cost-effectiveness plane of the mean incremental probabilistic sensitivity analyses (PSA) results for the moderate intensity intervention compared with the 'do nothing' control in each of the six population subgroups. Crosses represent 95% confidence intervals for costs and quality-adjusted life-years (QALYs). FINDRISC, Finnish Diabetes Risk; SE, socio-economic status.

target or 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 impact on 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 short-term cost-savings.

HbA_{1c} > 42 mmol/mol (6%) and FINDRISC > 0.1 are the most effective subgroups to target to reduce diabetes diagnoses, and generate the greatest short- and long-term cost-savings, although targeting individuals with HbA_{1c} > 42 mmol/mol (6%) is a much more cost-effective strategy than targeting FINDRISC > 0.1.

The analysis described here includes several limitations due to 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. due to ease of recruitment), limiting our ability to make recommendations about which individuals should be targeted. Further research directed at subgroup analysis would be extremely useful to inform this parameter. More generally, the analysis assumed the reduction in metabolic trajectories following 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 base 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 [32]. However, we think this is unlikely to significantly alter the results at the population level.

We used the Framingham heart failure risk score to describe risk of heart failure in the model. This risk score is based on old data from the USA and may not be representative of the UK. However, we do not think that this limitation has impacted on our overall results. Sensitivity analyses confirmed that the model was moderately responsive to heart failure incidence, but it did not affect the conclusions of this article.

Our validation work indicates that the model may overestimate diabetes incidence in high impaired glucose regulation populations due to the structure of the model. It is possible that this may bias the results in favour of the HbA_{1c} risk group. However, there is a paucity of data on long-term diabetes incidence for different risk profiles to understand the extent of this limitation in our model.

The model could be developed in the future to describe dynamic changes in health behaviours and a broader range of health outcomes to improve model flexibility and decision-making. Smoking is included in the model as risk factor for HbA_{1c}, systolic blood pressure and CVD. We did not include a dynamic quit rate in the model and did not assume that the intervention was effective in improving smoking cessation compared with usual care. Including smoking cessation and current smoking cessation services would add considerable complexity to the model. Furthermore, we do not currently account for non-related healthcare costs that may impact on the results, particularly where interventions improve survival [33]. Current NICE guidelines do not require the inclusion of unrelated healthcare costs, however, we believe that the model would benefit from inclusion of other health outcomes, such as dementia.

Two previous UK-based economic evaluations have found that lifestyle interventions for diabetes prevention are cost-effective but not cost-saving in subgroups with either low socio-economic status or high diabetes risk score and HbA_{1c} > 42 mmol/mol (6%) [3,4]. The results from the SPHR model are broadly similar. The QALY gains for the individuals receiving the intervention in the HbA_{1c} > 42 mmol/mol (6%) group are of similar magnitude to NICE public health guidance PH38 [4]. We believe that several factors explain the differences in incremental costs. First, 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. Second, the costs of major events, such as CVD have increased due to inflation. Third, the cost of screening individuals for Type 2 diabetes to identify individuals at high risk due to hyperglycaemia was not included in this version of the SPHR model.

The main drivers of the model are the impact of the intervention in reducing diabetes and CVD. A substantial proportion of incremental costs can be attributed to the diabetes and CVD-related cost-saving (Supporting Information File S3). The deterministic sensitivity analyses highlight that the model results are most sensitive to changes in the baseline incidence of these conditions.

In our 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 policymakers 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. Data inputs and uncertainty distributions.
File S3. Supplementary results.
File S4. One-way sensitivity analyses.