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Estimating the population impact of screening strategies for identifying and treating people at high risk of cardiovascular disease: modelling study

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ABSTRACT

Objective To estimate the potential population impact of different screening strategies for identifying and treating people at high risk of cardiovascular disease, including strategies using routine data for cardiovascular risk stratification, in light of the UK government's recommended national strategy to screen all adults aged 40-74 for cardiovascular risk.

Design Modelling study using data from a prospective cohort, EPIC-Norfolk (European Prospective Investigation of Cancer-Norfolk).

Setting An English county.

Participants 16 970 men and women aged 40-74 and free from cardiovascular disease and diabetes at baseline.

Main outcome measures The main outcomes were the population attributable fraction, the number needed to screen to prevent one new case of cardiovascular disease, the number needed to treat to prevent one new case of cardiovascular disease, and the number of new cardiovascular events that could be prevented. Relative risk reductions for estimated treatment effects were derived from meta-analyses of clinical trials or guidelines from the National Institute for Health and Clinical Excellence.

Results 1362 cardiovascular events occurred over 183 586 person years of follow-up. Compared with the recommended government strategy, a stepwise screening approach using a simple risk score incorporating routine data could prevent a similar number (lower to upper estimates) of new cardiovascular events annually in the United Kingdom (26 789, 20 778 to 36 239) and 25 134 (19 450 to 34 134), respectively) but requiring only 60% of the population to be invited to attend a vascular risk assessment. A similar number of cardiovascular events (25 016, 19 563 to 33 372) could also be prevented by inviting everyone aged 50-74 for a vascular assessment. Using a participant completed Finnish diabetes risk score questionnaire or anthropometric cut-off points for risk prestratification was less effective.

Conclusions Compared with the UK government's recommended national strategy to screen all adults aged 40-74 for cardiovascular risk, an approach using routine data for cardiovascular risk stratification before inviting people at high risk for a vascular risk assessment may be similarly effective at preventing new cases of cardiovascular disease, with potential cost savings.

INTRODUCTION

Primary prevention strategies have contributed to a major decline in the incidence of cardiovascular disease since the 1990s.[1] However, cardiovascular disease remains the leading cause of morbidity and mortality in the United Kingdom.[2] It is estimated to cost the UK economy £30bn (€34bn; $46bn) annually, about half of which is due to direct healthcare costs.[3] In an attempt to reduce the burden of cardiovascular disease further, the Department of Health has introduced a national vascular risk screening programme to identify those at high risk of cardiovascular disease.[4 5] All adults aged 40-74 and free of diabetes and cardiovascular disease and not being treated for hypertension who have never been identified by self assessment or record based screening will be invited to their surgery to attend a health check, including blood pressure measurement, blood tests, and cardiovascular risk assessment before the consideration of interventions appropriate to the level of risk.[5] It is estimated that the programme has the potential to prevent 9500 myocardial infarctions and strokes each year at an estimated annual cost of £250m.[4] These figures are, however, largely based on modelling studies using cross sectional data, with several key assumptions.[6 7] The costs and benefits associated with mass screening for cardiovascular disease are unknown.[8 9]

An alternative approach to inviting all eligible adults for vascular risk screening might be to prestratify people using routine data before inviting those at high risk to attend for the more invasive and expensive vascular risk assessment. This may reduce the number of people required to attend their surgery as well as the cost of the screening programme. This stepwise approach may also reduce the potential psychological harms, such as anxiety and false reassurance, that have been associated with screening tests.[10] Simple risk scores using routine data have been shown to predict cardiovascular disease[11 12] and all cause mortality.[12 13]

Whether this stepwise approach for risk stratification might have a similar impact on the prevention of new cases of cardiovascular disease compared with the recommended strategy is unknown.

Population impact measures can be used to estimate the effect of preventive strategies and interventions on health outcomes at the population level[14] and are therefore useful for informing public health decision making. Using data from a population based prospective UK cohort, we modelled different screening strategies to identify those at high risk of cardiovascular disease and we examined the potential population impact of each strategy by calculating the population attributable fraction, the number needed to screen to prevent one new case of cardiovascular disease, the number needed to treat with lifestyle or drug interventions to prevent one new case of cardiovascular disease, and the number of new cardiovascular events that could be prevented.

METHODS

The European Prospective Investigation of Cancer-Norfolk (EPIC-Norfolk) is a population based prospective study of men and women aged 40-79 residing in the county of Norfolk, United Kingdom. Details of the study have been described elsewhere.[15] Briefly, between 1993 and 1997, 77 630 adults were invited from general practice to participate in the study. Of these, 25 639 (33.0%) consented and attended a baseline health assessment. Participants completed questionnaires about their personal and family history of disease, drug use, and lifestyle, including smoking. Participants were also asked whether a doctor had ever told them that they had any of the conditions in a list that included diabetes, myocardial infarction ("heart attack"), and stroke. Self reported physical activity was measured using the European Prospective Investigation of Cancer physical activity questions,[16] which includes questions on both occupational and recreational physical activity as well as time spent in each activity. It has been validated against objectively measured physical activity.[16] Dietary behaviour was measured using a seven item questionnaire on consumption of vegetables and fruits.[17] Self reported consumption of these foods has been associated with cardiovascular risk both in the EPIC-Norfolk cohort[18] and in other similar longitudinal studies.[19 20] Anthropometric and blood pressure measurements and non-fasting blood samples were also taken at the health assessment.

People living in the Norfolk area are healthier than the general UK population, with a standardised mortality ratio of 93.[21] However, EPIC-Norfolk is similar to a nationally representative sample for anthropometric indices, blood pressure measurements, and serum lipid levels.[15]

We followed up participants who were free from cardiovascular disease and diabetes at the time of recruitment, for the development of a first cardiovascular event or death. We report results for follow-up to 30 April 2007, a median of 10 years. Incident cardiovascular disease was defined as a composite of fatal or non-fatal cardiovascular disease, including admission to hospital for coronary heart disease or stroke, or death from coronary heart disease, stroke, or peripheral vascular disease. We used the participants' National Health Service number to determine their hospital stay through the East Norfolk Health Authority database, which records all hospital contacts throughout England and Wales for Norfolk residents. Vital status for all EPIC-Norfolk participants was obtained through death certification at the Office for National Statistics. Previous validation studies in this cohort indicated high specificity of such case ascertainment.[22]

Statistical analysis

We summarised the baseline characteristics separately for men and women with and without cardiovascular disease, using percentages for categorical data, means for normally distributed data, and medians for non-normally distributed data. We tested for differences between groups using χ^2 tests for categorical variables and *t* tests or Kruskal-Wallis tests for normally or non-normally distributed continuous variables. To calculate cardiovascular event rates we divided the number of such events by person years of follow-up. Follow-up was defined as the period from the date of first health assessment to the date of the first event (admission to hospital or death), or 30 April 2007.

Modelling screening strategies

In keeping with guidelines proposed by the national screening committee, we limited our analyses to people aged 40-74 (779 people excluded) and excluded those with a history of cardiovascular disease (n=1015), with prevalent diabetes (n=704), and taking lipid lowering drugs (n=241) or antihypertensive drugs, including diuretics (n=3488). We tested the ability of screening strategies incorporating different risk scores to identify those at high risk of cardiovascular disease—the Framingham risk score,[11] the Cambridge diabetes risk score,[23] and the Finnish diabetes risk score.[24] We used the Cambridge risk score solely as an example of a risk score using data routinely available in general practice records, and the Finnish diabetes risk score as an example of a participant completed questionnaire (recommended by the Department of Health as a first step for identifying people at high risk, who will be offered testing for fasting blood glucose). People with missing values for one or more of the variables used to calculate these scores were also excluded (n=2442), leaving 16 970 people for analysis.

The Framingham risk score was derived using the modified Framingham risk functions, recently updated by D'Agostino et al.[11] The Cambridge risk score, a tool developed in a British population to identify people at risk of undiagnosed diabetes,[23] was derived using data on age, sex, smoking, family history of diabetes, body mass index, and prescribed steroids and antihypertensive drugs, variables that are routinely available in primary care. We previously showed that this score was effective at identifying people with diabetes who have a raised and potentially modifiable risk of coronary heart disease,[25] and at predicting all cause mortality.[13]

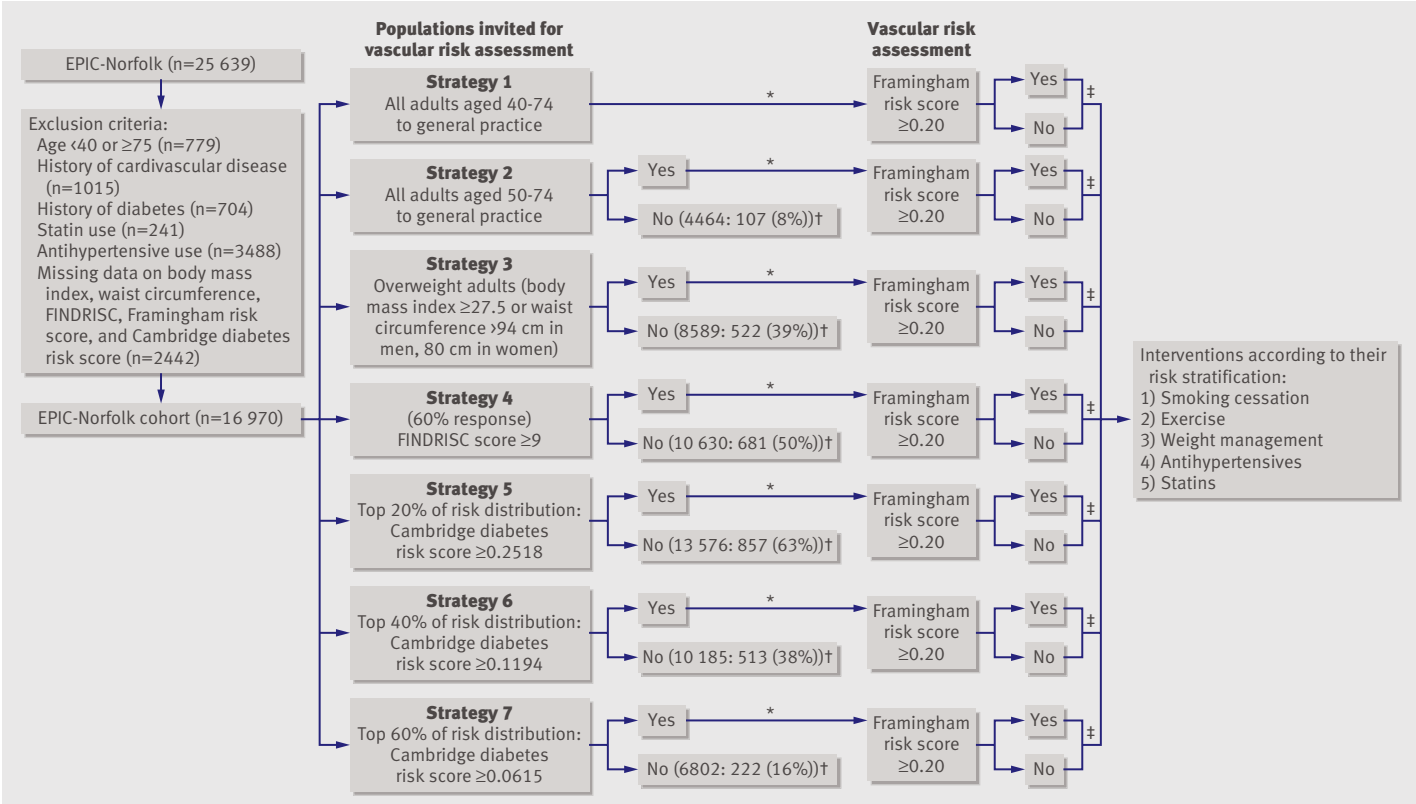
The Finnish diabetes risk score questionnaire is a simple tool, developed in a Finnish cohort, and includes age; self reported use of antihypertensive drugs; history of high blood glucose levels; physical activity of at least four hours a week; daily consumption of vegetables, fruits, and berries; and self reported body mass index and waist circumference.[24] It has been shown to predict incident coronary heart disease, stroke, and total mortality in a Finnish population.[12] The Department of Health plans to incorporate this risk score in the vascular screening programme to identify people who need further testing of blood glucose levels.[4]

We assumed that the response rate to the self administered Finnish diabetes risk score questionnaire was 60%. We used a simple ordered index of overall physical activity derived from the baseline European Prospective Investigation of Cancer physical activity questions,[16] which is associated with incident cardiovascular disease and all cause mortality in the EPIC-Norfolk cohort.[26] We used a simple seven item question about consumption of vegetables and fruits to examine whether participants in the cohort consumed vegetables, fruit, or berries daily. As data on history of high blood glucose levels were not available in EPIC-Norfolk, we decided to exclude this variable in the calculation of the Finnish diabetes risk score. We carried out a sensitivity analysis for different response rates to the Finnish diabetes risk score questionnaire (40% and 80%) and for its extreme cut-off points of 12 and 7, assuming, respectively, that nobody had a history of hyperglycaemia and that everyone had a history of hyperglycaemia. We also carried out a sensitivity analysis to examine whether the population impact of the strategies incorporating routine data (Cambridge risk score) might change after excluding family history of diabetes, smoking, or body mass index from the score.

We modelled seven different stepwise population based strategies to screen for cardiovascular disease (figure).

Stage 1: populations to be invited for vascular risk assessment

- Strategy 1—all adults aged 40-74 (Department of Health recommendation)
- Strategy 2—all adults aged 50-74
- Strategy 3—overweight adults (defined by body mass index ≥27.5 kg/m^2 or a waist circumference >94 cm in men and >80 cm in women)
- Strategy 4 (high risk approach using a participant completed questionnaire)—adults with a score of ≥9 on the Finnish diabetes risk score questionnaire
- Strategies 5-7 (high risk approach using routinely available data)—adults ranked according to their



FINDRISC = Finnish diabetes risk score
* 75% attend for vascular risk assessment
† Numbers in parentheses are number of people not invited for vascular risk assessment, number of those who developed cardiovascular disease in this group (% of total)
‡ Stratified by obesity, smoking, hypertension, and high or low cardiovascular disease risk according to Framingham risk score with different rates of uptake, adherence, and relative risk reduction for each intervention

Schematic diagram of population based strategies to screen for cardiovascular disease, and subsequent interventions

Table 1 | Uptake, compliance, and relative risk reduction for interventions based on published literature and expert opinion[6]

Intervention	Uptake (%)	Compliance (%)	Relative risk reduction of cardiovascular disease
Smoking cessation	19	15	0.36*
Antihypertensives	40	87	0.24†
Statins	85	70	0.31‡
Weight management	85	68	0.36§

*From meta-analysis on effect of smoking cessation on mortality and non-fatal cardiovascular disease.[27]
†From NICE guidelines CG18 and CG34.[28]
‡From NICE guideline TA94.[29]
§From clinical trial of weight reducing diet and exercise.[30]

Cambridge risk score using data from their electronic general practice records; those in the top 20%, 40%, and 60% of the risk distribution would be invited

Stage 2

It was assumed that 75% of people invited would attend a vascular risk assessment,[6] which would include medical history taking, a physical examination, and blood tests, as recommended by the national screening committee. These measurements would then be used to calculate a Framingham risk score for each participant. The national screening committee recommends that these people would then be stratified into high and low risk groups according to their Framingham risk score (high risk: Framingham risk score ≥0.20), whether they were obese, hypertensive, or current smokers. People would receive interventions appropriate to their risk level, based on the assumptions of uptake, adherence, and relative risk reduction, as outlined in a recent report from the Department of Health's vascular team[6] (table 1). For example, someone who was obese, hypertensive, and had a Framingham risk score ≥0.20 would be offered a weight management programme and treatment with antihypertensives and statins.

For each screening strategy we estimated the cumulative incidence rate of cardiovascular disease, the sensitivity or specificity, the area under the receiver operating characteristic curve for the prediction of cardiovascular disease, the population attributable fraction, the number needed to screen to prevent one new case of cardiovascular disease, the number needed to treat to prevent one new case of cardiovascular disease, and the number of cardiovascular events that could be prevented in the population.[31 32] Sensitivity is the proportion of those who developed cardiovascular disease who were correctly identified as "high risk" by each screening strategy (combination of prestratification and then the second step risk assessment). Specificity refers to the proportion of the population that did not experience a cardiovascular event who were correctly identified as "low risk" by each strategy. The area under the receiver operating characteristic curve represents the ability of each screening strategy to discriminate between those who did and those who did not develop a cardiovascular event, with a higher value suggesting better discriminatory ability. The population attributable fraction quantifies the contribution of each screening strategy to the prevention of cardiovascular disease—that is, it represents the additional proportion of cardiovascular events that could be prevented in the population if a screening strategy was implemented, compared with no screening strategy. After adults were stratified into groups according to their level of cardiovascular risk, we applied uptake and compliance rates and relative risk reduction for each prevention intervention to calculate the number of cardiovascular events that could be prevented in each group (box). The number of cardiovascular events that could be prevented in the population is the sum of the number of cardiovascular events that could be prevented in all the groups.

We also modelled the population impact for situations where 65% and 85% of those invited would attend a vascular risk assessment. For demonstrative purposes, we also calculated the number of cardiovascular events that could be prevented in the population for an average primary care trust with a catchment area including 136 900 people aged 40-74 and for the UK population, using population estimates for mid-2007.[33] For the purpose of modelling the population impact of different cardiovascular disease screening strategies and interventions, we made several assumptions (box). Owing to uncertainty concerning the interaction between multiple interventions, we also did a sensitivity analysis for the situation where there was no

Assumptions for modelling population impact of different population based screening strategies for cardiovascular disease and primary prevention interventions

Everyone invited to a vascular assessment has an equal attendance rate (response rate 75%)[6]

Risk of cardiovascular mortality is considered to be equal in those who do and those who do not attend for screening

Nobody is receiving any intervention at baseline

If someone takes up two or more interventions, the relative risk will be multiplicative. Therefore, combined relative risk can be calculated[6]:

$$\text{cardiovascular disease risk}_{(new)} = \text{cardiovascular disease risk}_{(prior)} \times (1-\text{relative risk reduction})_{int\_1} \times (1-\text{relative risk reduction})_{int\_2} \times \ldots \times (1-\text{relative risk reduction})_{int\_n}$$

Screening and interventions are assumed to occur only once

Adults who do not complete the intervention are assumed to have a cardiovascular risk similar to those who never received an intervention

All lifestyle and drug interventions are independent of each other, so the rate of taking up and adhering to one intervention does not have an effect on uptake and adherence to another intervention[6 7]

According to the previous assumptions, the number of cardiovascular events that could be prevented in the population can be calculated[31 32]:

$$\text{number of cardiovascular events that could be prevented in the population} = N \times \text{cardiovascular disease rate}_{(prior)} \times (1-((1-pt \times pa \times \text{relative risk reduction})_{int\_1} \times (1-pt \times pa \times RRR)_{int\_2} \times \ldots \times (1-pt \times pa \times \text{relative risk reduction})_{int\_n}))$$

where N=number of people eligible for receiving multiple intervention; cardiovascular disease rate$_{(prior)}$=background cardiovascular disease rate without intervention; pt=proportion of people taking up intervention (uptake rate); pa=proportion of people adhering to intervention (compliance); int_1=intervention 1; int_n=intervention n

Lower and upper estimates of the number of cardiovascular events that could be prevented in the population are calculated by applying point estimates of pt, pa, and relative risk reduction to cardiovascular disease rate, with 95% confidence interval

additive effect between interventions—that is, the relative risk reduction for multiple interventions was equal to that of the single intervention with the largest risk reduction.

RESULTS

Table 2 summarises the baseline characteristics of the EPIC-Norfolk cohort. The median age of participants was 56 years (interquartile range 49 to 64), and 7505 (44%) were men. Participants who developed cardiovascular disease during follow-up were older, more obese, had higher blood pressure and cholesterol and HbA_{1c} levels, and had lower high density lipoprotein cholesterol levels than those who did not develop cardiovascular disease. They were less likely to be moderately active or active and to consume vegetable and fruits on a daily basis. The median values of the Framingham and Cambridge risk scores were higher in those who developed cardiovascular disease compared with those who did not (Framingham risk score 0.21 *v* 0.10, P<0.001, Cambridge risk score 0.17 *v* 0.08, P<0.001). The Finnish diabetes risk score was also higher in those who developed cardiovascular disease (median score 8.5 *v* 7.0, P<0.001).

Overall, 1362 cardiovascular events occurred over 183 586 person years of follow-up. The incidence rate of cardiovascular disease was 7.4 per 1000 person years. The incidence rate was higher in men than in women (11.0, 95% confidence interval 10.2 to 11.7 *v* 4.7, 4.3 to 5.2 per 1000 person years). The incidence rate in those with a Framingham risk score of ≥0.20 was 19.4 (18.1 to 20.9) per 1000 person years, whereas in those with a Framingham risk score of <0.20 it was 4.3 (4.0 to 4.7) per 1000 person years.

Table 3 shows for each strategy the number of people who would need to be invited to a vascular risk assessment, the risk of cardiovascular disease, the sensitivity and specificity, and the predictive ability. If adults aged 50 or more were invited to a vascular risk assessment (strategy 2), three quarters of the total population aged 40-74 would receive invitations. About half the population would need inviting for risk assessment if body mass index and waist circumference cut-off points were used for risk

Table 2 | Baseline characteristics of EPIC-Norfolk cohort by cardiovascular disease (CVD) outcome and sex, 1993-2007. Values are numbers (percentages) unless stated otherwise

	Men			Women		
Characteristics	Did not develop CVD	Developed CVD	P value*	Did not develop CVD	Developed CVD	P value*
No of participants	6634	871		8974	491	
Median (interquartile range) age (years)	55 (49-63)	63 (55-68)	<0.001	55 (49-63)	66 (58-70)	<0.001
Social class†:						
Professional	558 (8.5)	52 (6.1)	0.006	638 (7.3)	18 (3.8)	0.015
Managerial	2589 (39.5)	320 (37.5)		3257 (37.0)	173 (36.4)	
Skilled, non-manual	781 (11.9)	107 (12.5)		1683 (19.1)	109 (22.9)	
Skilled, manual	1642 (25.0)	210 (24.6)		1826 (20.8)	94 (19.8)	
Semiskilled	823 (12.6)	131 (15.4)		1096 (12.5)	58 (12.2)	
Non-skilled	163 (2.5)	33 (3.9)		296 (3.4)	23 (4.8)	
Mean (SD) body mass index	26.1 (3.1)	26.7 (3.4)	<0.001	25.7 (4.0)	26.4 (4.2)	<0.001
Mean (SD) waist circumference (cm)	94.2 (9.2)	96.4 (9.8)	<0.001	80.4 (10.0)	84.2 (10.5)	<0.001
Mean (SD) systolic blood pressure (mm Hg)	134.2 (16.0)	142.4 (18.4)	<0.001	130.5 (17.7)	140.1 (18.3)	<0.001
Mean (SD) diastolic blood pressure (mm Hg)	83.3 (10.4)	86.7 (11.8)	<0.001	79.6 (10.7)	83.6 (11.0)	<0.001
Mean (SD) total cholesterol level (mmol/l)	5.9 (1.1)	6.3 (1.1)	<0.001	6.2 (1.2)	6.7 (1.2)	<0.001
Mean (SD) high density lipoprotein level (mmol/l)	1.25 (0.33)	1.20 (0.32)	0.002	1.59 (0.44)	1.49 (0.42)	<0.001
Mean (SD) HbA_{1c} (%)	5.2 (0.6)	5.4 (0.8)	<0.001	5.1 (0.6)	5.5 (0.8)	<0.001
Smoking status:						
Non-smoker	2468 (37.2)	239 (27.4)	<0.001	5159 (57.5)	246 (50.1)	<0.001
Former smoker	3375 (50.9)	477 (54.8)		2755 (30.7)	158 (32.2)	
Current smoker	791 (11.9)	155 (17.8)		1060 (11.8)	87 (17.7)	
Moderately active and active	3328 (50.2)	391 (44.9)	0.003	3804 (42.4)	149 (30.4)	<0.001
Daily consumption of vegetables and fruits	3261 (49.2)	398 (45.7)	0.055	5818 (64.8)	281 (57.2)	0.001
Median (interquartile range) FINDRISC score	7 (4-10)	8 (6-11)	<0.001	7 (4-10)	9 (6-11)	<0.001
Median (interquartile range) diabetes risk score	0.13 (0.07-0.27)	0.20 (0.11-0.42)	<0.001	0.05 (0.02-0.13)	0.10 (0.05-0.27)	<0.001
Median (interquartile range) Framingham risk score	0.16 (0.10-0.25)	0.26 (0.18-0.35)	<0.001	0.07 (0.04-0.12)	0.14 (0.09-0.21)	<0.001

FINDRISC=Finnish diabetes risk score.
*Difference between people who developed cardiovascular disease and those who did not using *t* tests or Kruskal-Wallis tests for normally or non-normally distributed continuous variables and χ^2 tests for categorical variables.
†Numbers do not add up to total as 290 people had missing data for this variable.

Table 3 | Comparison of sensitivity, specificity, and predictive ability of different screening strategies for cardiovascular disease in EPIC-Norfolk cohort

Screening strategy	No invited for risk assessment (%)	CVD events in risk group (%)	Person years at risk	Incidence of CVD per 1000 person years (95% CI)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Area under ROC (95% CI)
Overall							
Total	16 970	1362	183 586	7.42 (7.04 to 7.82)	NA	NA	NA
Men	7505	871	79 517	10.95 (10.25 to 11.71)			
Women	9465	491	104 068	4.72 (4.32 to 5.15)			
Strategy 1: all adults							
Total	16 970 (100)	1362 (100)	183 586	7.42 (7.04 to 7.82)	53.9 (51.2 to 56.6)	80.7 (80.1 to 81.3)	0.67 (0.66 to 0.69)
Men	7505 (100)	871 (100)	79 517	10.95 (10.25 to 11.71)	68.8 (65.6 to 71.8)	64.5 (63.3 to 65.7)	0.67 (0.65 to 0.68)
Women	9465 (100)	491 (100)	104 068	4.72 (4.32 to 5.15)	27.5 (23.6 to 31.7)	92.6 (92.1 to 93.2)	0.60 (0.58 to 0.62)
Strategy 2: age ≥50 years							
Total	12 506 (74)	1255 (92)	134 276	9.35 (8.84 to 9.88)	52.6 (49.9 to 55.2)	82.0 (81.4 to 82.6)	0.67 (0.66 to 0.68)
Men	5641 (75)	793 (91)	59 099	13.42 (12.52 to 14.39)	66.8 (63.6 to 69.9)	65.6 (64.4 to 66.7)	0.66 (0.65 to 0.68)
Women	6865 (73)	462 (94)	75 177	6.15 (5.61 to 6.73)	27.3 (23.4 to 31.5)	92.7 (92.1 to 93.2)	0.60 (0.58 to 0.62)
Strategy 3: body mass index and waist circumference							
Total	8381 (49)	840 (62)	89 282	9.41 (8.79 to 10.07)	35.1 (32.6 to 37.7)	87.5 (87.0 to 88.0)	0.61 (0.60 to 0.63)
Men	3895 (52)	532 (61)	40 530	13.13 (12.06 to 14.39)	43.1 (39.7 to 46.4)	77.8 (76.7 to 78.7)	0.60 (0.59 to 0.62)
Women	4486 (47)	308 (63)	48 753	6.32 (5.65 to 7.06)	21.0 (17.5 to 24.9)	94.7 (94.2 to 95.1)	0.58 (0.56 to 0.60)
Strategy 4: FINDRISC ≥9							
Total	6340 (37)	681 (50)	67 154	10.14 (9.41 to 10.93)	29.9 (27.5 to 32.4)	89.0 (88.5 to 89.5)	0.59 (0.58 to 0.61)
Men	2812 (37)	413 (47)	28 985	14.25 (12.94 to 15.69)	35.2 (32.1 to 38.5)	80.7 (79.7 to 81.7)	0.58 (0.56 to 0.60)
Women	3528 (37)	268 (55)	38 169	7.02 (6.23 to 7.91)	20.4 (16.9 to 24.3)	95.1 (94.6 to 95.5)	0.58 (0.56 to 0.60)
Strategy 5: top 20% of CRS							
Total	3394 (20)	505 (37)	35 049	14.41 (13.20 to 15.72)	26.1 (23.8 to 28.5)	91.8 (91.3 to 92.2)	0.59 (0.58 to 0.60)
Men	2176 (29)	374 (43)	22 191	16.85 (15.23 to 18.65)	34.6 (31.4 to 37.8)	84.3 (83.4 to 85.1)	0.59 (0.58 to 0.61)
Women	1218 (13)	131 (27)	12 858	10.19 (8.58 to 12.09)	11.0 (8.4 to 14.2)	97.3 (96.9 to 97.6)	0.54 (0.53 to 0.56)
Strategy 6: top 40% of CRS							
Total	6785 (40)	849 (62)	71 162	11.93 (11.15 to 12.76)	41.6 (39.0 to 44.3)	85.6 (85.1 to 86.2)	0.64 (0.62 to 0.65)
Men	4088 (54)	625 (72)	42 164	14.82 (13.71 to 16.03)	55.9 (52.5 to 59.2)	71.7 (70.6 to 72.8)	0.64 (0.62 to 0.66)
Women	2697 (28)	224 (46)	28 998	7.72 (6.78 to 8.81)	16.3 (13.2 to 19.9)	95.9 (95.5 to 96.3)	0.56 (0.54 to 0.58)
Strategy 7: top 60% of CRS							
Total	10 168 (60)	1140 (84)	107 939	10.56 (9.97 to 11.19)	52.0 (49.3 to 54.7)	81.7 (81.1 to 82.3)	0.67 (0.65 to 0.68)
Men	5875 (78)	802 (92)	61 512	13.04 (12.17 to 13.97)	67.4 (64.2 to 70.5)	65.3 (64.1 to 66.4)	0.66 (0.65 to 0.68)
Women	4293 (45)	338 (69)	46 427	7.28 (6.54 to 8.10)	24.6 (20.9 to 28.7)	93.8 (93.3 to 94.3)	0.59 (0.57 to 0.61)

FINDRISC=Finnish diabetes risk score; CRS=Cambridge diabetes risk score, ROC=receiver operating characteristic curve.

prestratification (strategy 3) and only 37% for the strategy using a participant completed questionnaire—Finnish diabetes risk score cut-off point of ≥9 (strategy 4). The strategies of inviting people aged 50-74 and using routine data (60% Cambridge risk score) were the most effective at identifying those who developed a first cardiovascular event. Both strategies identified the highest proportion of people who developed a first cardiovascular event (92% and 83%, respectively). In contrast, using a participant completed questionnaire (strategy 4) identified 50% of those who developed a cardiovascular event.

Inviting adults aged 50 or more (strategy 2) did not compromise the sensitivity, specificity, or predictive ability for cardiovascular events, compared with inviting everyone (strategy 1). Strategy 7 also showed comparable sensitivity and specificity, with a similar ability to predict cardiovascular disease compared with strategy 1: area under the receiver operating characteristic curve 0.67 (95% confidence interval 0.65 to 0.68) and 0.67 (0.66 to 0.69), respectively. In contrast, inviting people who are overweight and those at high risk using a participant completed questionnaire (strategies 3 and 4) had significantly lower predictive abilities.

Table 4 shows the potential population impact of the different screening strategies and subsequent treatment options. The population attributable fraction was greatest for strategies using age 50 or more and routine data (60% Cambridge risk score) for identifying people at risk, whereas inviting people who were overweight and those at high risk using a participant completed questionnaire (strategies 3 and 4) had the lowest population attributable fractions. When using the Cambridge risk score to rank people before inviting those at high risk for a vascular risk assessment (strategy 5-7), both the population attributable fraction and the number of cardiovascular events that could be prevented in the population increased with the increasing number of people invited. Strategy 1 would prevent the highest number of new cardiovascular events

with a number of cardiovascular events that could be prevented in the population of 16.9, whereas strategies 2 and 7 had slightly lower values, of 15.7 and 15.8, respectively. However, the number needed to attend vascular risk assessment to prevent one cardiovascular event was lower for strategies 7 and 2 compared with strategy 1 (482, 596, and 755, respectively). When applying the number of cardiovascular events that could be prevented in the population to the UK population in mid-2007, 26 789 new cardiovascular events could be prevented each year if all adults aged 40-74 were invited for a vascular risk assessment, whereas 25 134 new cases could be prevented if 60% of people at high risk according to the Cambridge risk score were invited for a vascular risk assessment.

In a sensitivity analysis, when the response rate to the participant completed questionnaire (Finnish diabetes risk score) was 40%, the number of new cardiovascular events that could be prevented was 6724, and when a higher response rate of 80% was achieved, this strategy could prevent 13 449 new cardiovascular events. Using a Finnish diabetes risk score cut-off point of 7 or more (assuming everyone had a history of hyperglycaemia) identified 70% of those who developed cardiovascular disease, and this approach could prevent 21 114 new cardiovascular events. Using a Finnish diabetes risk score cut-off point of 12 or more (equivalent to the situation where nobody had a history of hyperglycaemia) identified only 18% of those who developed cardiovascular disease, and this strategy had the lowest population attributable fraction and number of cardiovascular events that could be prevented in the population; only 7259 new cases could be prevented. The number of new cardiovascular events that could be prevented when attendance rates were changed from 65% to 85% increased from 23 217 to 30 361 cases for the strategy inviting everyone, and from 21 783 to 28 485 cases for the high risk approach using routine data (60% Cambridge risk score). Finally, excluding family history of diabetes, smoking, or body mass index from the Cambridge risk score did not significantly reduce the population impact of the strategies using routine data as a prestratification tool. When no additive effect between interventions was

Table 4 | Comparison of potential population impact of different cardiovascular disease (CVD) screening strategies and interventions in EPIC-Norfolk cohort (n=16 970)

Screening strategy	Population attributable fraction (%)	No needed to attend risk assessment to prevent one new CVD event	No needed to intervene to prevent one new CVD event	NEPP (lower to upper estimates)	NEPP for average primary care trust* (lower to upper estimates)	NEPP for United Kingdom† (lower to upper estimates)
Strategy 1: all adults						
Total	100	755	107	16.9 (13.1 to 22.8)	136 (106 to 184)	26 789 (20 778 to 36 239)
Men	100	449	75	12.5 (10.1 to 16.0)	101 (81 to 129)	19 904 (16 044 to 25 377)
Women	100	1638	199	4.3 (3.0 to 6.8)	35 (24 to 55)	6885 (4734 to 10 862)
Strategy 2: age ≥50 years						
Total	71	596	95	15.7 (12.3 to 21.0)	127 (99 to 169)	25 016 (19 563 to 33 372)
Men	65	360	68	11.8 (9.6 to 14.8)	95 (77 to 119)	18 681 (15 192 to 23 444)
Women	79	1291	176	4.0 (2.8 to 6.3)	32 (22 to 50)	6335 (4372 to 9927)
Strategy 3: body mass index and waist circumference						
Total	25	527	100	11.9 (9.0 to 16.7)	96 (73 to 135)	18 950 (14 332 to 26 555)
Men	21	340	68	8.6 (6.8 to 11.3)	69 (55 to 91)	13 637 (10 766 to 17 879)
Women	30	1006	184	3.3 (2.2 to 5.5)	27 (18 to 44)	5313 (3566 to 8676)
Strategy 4: FINDRISC ≥9						
Total	21	449	96	6.4 (4.8 to 9.0)	51 (38 to 73)	10 087 (7551 to 14 322)
Men	17	282	63	4.5 (3.5 to 5.9)	36 (28 to 48)	7124 (5577 to 9443)
Women	28	851	173	1.9 (1.2 to 3.1)	15 (10 to 25)	2962 (1962 to 4879)
Strategy 5: top 20% of CRS						
Total	22	300	68	8.5 (6.2 to 12.3)	68 (50 to 99)	13 456 (9921 to 19 566)
Men	21	245	54	6.7 (5.1 to 9.0)	54 (41 to 73)	10 591 (8151 to 14 308)
Women	16	506	118	1.8 (1.1 to 3.3)	15 (9 to 27)	2865 (1770 to 5258)
Strategy 6: top 40% of CRS						
Total	38	390	85	13.1 (10.0 to 18.0)	105 (80 to 146)	20 731 (15 838 to 28 659)
Men	40	298	63	10.3 (8.2 to 13.3)	83 (66 to 107)	16 318 (12 979 to 21 148)
Women	25	728	167	2.8 (1.8 to 4.7)	22 (15 to 38)	4413 (2859 to 7511)
Strategy 7: top 60% of CRS						
Total	60	482	91	15.8 (12.2 to 21.5)	128 (99 to 173)	25 134 (19 450 to 34 134)
Men	65	362	69	12.2 (9.8 to 15.5)	98 (79 to 125)	19 320 (15 553 to 24 678)
Women	44	880	166	3.7 (2.5 to 6.0)	30 (20 to 48)	5814 (3897 to 9456)

NEPP=number of new CVD events that could be prevented; FINDRISC=Finnish diabetes risk score; CRS=Cambridge diabetes risk score.
*Catchment area 136 900 adults aged 40-74.
†26 954 900 adults aged 40-74.

assumed, the number of cardiovascular events prevented for each strategy was reduced, but relative comparisons between strategies using routine data and the strategy of inviting everyone remained unchanged.

DISCUSSION

We estimated the potential population impact of different screening strategies for identifying people at high risk of cardiovascular disease before lifestyle and drug intervention. Compared with the recently recommended programme by the national screening committee, our findings suggest that a similar number of new cardiovascular events could be prevented by using routine data to prestratify people before inviting those at high risk to the more invasive and expensive vascular risk assessment.

This approach has the potential to reduce the number of people required to attend their surgery for vascular risk screening, as well as the cost of the screening programme. A similar benefit could also be achieved if vascular risk assessments were limited to adults aged 50 or more.

Strategies using a participant completed questionnaire (Finnish diabetes risk score) or anthropometric measures as prestratification tools seem to have a lesser impact on primary prevention of cardiovascular disease at the population level.

Comparison with other studies

Although several studies have examined the impact of a single intervention on prevention of cardiovascular disease,[34-36] few studies have examined the population impact of integrated multifactorial prevention strategies on reducing the burden of cardiovascular disease.

A modelling study by Gemmell et al estimated the population impact of strategies to prevent coronary heart disease in England using aggregate data.[31] They found that an estimated 4410 cases of coronary heart disease could be prevented each year by lifestyle interventions and 2008 by drug interventions. These numbers are lower than our findings. This might be explained by the individual level data used in our study, which more closely represent real life situations for population cardiovascular risk. Another explanation might be the difference in the definition of outcomes and the relative risk reduction estimates used in each study.

Kahn et al used the Archimedes model to simulate the population impact and cost effectiveness of 11 interventions for cardiovascular disease prevention in the US population, using individual level data from the national health and nutrition education survey.[37] They found that with feasible levels of performance and effectiveness of implementing all prevention interventions together, 36% of myocardial infarctions and 20% of strokes could be prevented over 30 years. However, they did not consider screening procedures to identify those at high risk and to whom interventions should be targeted.

A modelling study by Marshall and Rouse[38] found similar results to our own. They suggest that strategies preselecting patients for risk assessment may reduce staff time and prevent more new cases within available resources, compared with inviting everyone. However, the authors used a hypothetical population, assuming default blood pressure and blood cholesterol values for each individual, and calculated cardiovascular disease risk using the Framingham equations to identify those at high risk who should be invited for cardiovascular risk assessment.

The Department of Health has recently published a report on the simulated population impact of various vascular risk screening programmes.[7] The effects of inviting different age groups and different intervals for repeating vascular checks were modelled, including a strategy to invite those at high risk for a vascular assessment. They report the greatest benefits and cost effectiveness for a strategy in which everyone aged 40-74 was invited for a vascular check every five years compared with other approaches. This contrasts with our findings, which suggest that a strategy inviting adults aged 50-74 or inviting just those identified as high risk using routine data could prevent a similar number of new cardiovascular events.

In the Department of Health report, the authors used cross sectional data from the QRESEARCH database and estimated cardiovascular risk using the QRISK and the Framingham risk score.[6 7] Our study used data from a prospective cohort, which allowed us to use actual rates for cardiovascular disease events. Moreover, not all risk factors for each individual were measured in the QRESEARCH database, so the authors used different datasets to simulate an individual patient's level of risk. Significant data were missing for some risk factors—for example, 72% of patients did not have data for cholesterol levels, and these values were imputed.[6]

Another explanation for the difference found between our study and the Department of Health report is our assumption that the offer of screening and subsequent interventions would occur only once. The Department of Health modelled screening and interventions with phased implementation repeated every five or 10 years and considered changes in risk factors and cardiovascular risk over time.[6 7]

Strengths and limitations of the study

We examined the potential population impact of different screening strategies and prevention interventions for cardiovascular disease in a large population based cohort, using robust cardiovascular disease outcomes over a long period. We used relevant measures of population impact such as the number needed to screen and the number of events that could be prevented in the population. Our modelling was based on actual rates of cardiovascular disease with associated 95% confidence intervals; key assumptions were informed by evidence from meta-analyses of clinical trials and were subject to sensitivity analyses to identify sources of uncertainty and to quantify their contribution to overall uncertainty.

However, using a single point estimate (deterministic approach) for rates of uptake, compliance, and relative risk reduction, without accounting for uncertainty of each estimate, limits insight into the range of these intervention related variables and underestimates the true uncertainty of the population impact. An alternative approach would be to use probabilistic risk assessment, which provides greater information on the variability and uncertainty associated with health risk and benefits by simultaneously accounting for the uncertainty of multiple variables.[39]

It is unlikely that people at different levels of cardiovascular risk have the same attendance rate. People at high risk are less likely to attend for screening—for example, older men are less likely to attend for screening than younger women.[40] We also assumed an equal risk of cardiovascular mortality in those who did and did not attend for screening, but previous studies have shown that those who do attend have a significantly lower mortality than those who do not attend.[41 42] However, although these assumptions may affect the number of events that could be prevented they are unlikely to alter the main finding that prestratification using routine data is more efficient than inviting all middle aged members of the population for vascular risk assessment.

Additionally, given the modest sensitivity of all the proposed strategies, it is possible that people who are not invited for assessment may be affected by adverse psychological symptoms such as insecurity and anxiety about the chance of developing the disease because they have been excluded from a screening programme.[43]

In our model, all interventions were understood to act independently of each other, but in practice the interaction between multiple lifestyle and drug interventions remains unclear. However, sensitivity analysis assuming no additive effect of interventions did not affect the relative performance of each screening strategy. The incidence of cardiovascular disease in many trials used to inform the assumptions for our modelling, particularly trials on lipid lowering,[44] is substantially higher than the risk in our study. As such, the reduction in cardiovascular risk associated with a particular intervention may not be fully achieved in this low risk population. Therefore, the estimates of the number of cardiovascular events that could be prevented might have been overestimated.

Lastly, as participants of EPIC-Norfolk are predominantly white, the generalisability of our findings to other ethnic groups and populations is limited. Ethnicity might be an additional factor on which decisions about how to invite high risk groups may be based.

Conclusions and policy implications

Understanding the balance between the benefits and costs of a screening programme is crucial for public health decision making. A universal screening programme for cardiovascular disease might prevent an important number of new cardiovascular events in a population, but it may be unrealistic to implement in increasingly resource constrained health systems. Policy makers have to decide on the balance between the number of people needed to screen or treat and the number of cases that can be prevented in the population.

Although data on body mass index and waist circumference are relatively inexpensive to collect and are increasingly available in primary care, using these anthropometric data for risk prestratification would fail to prevent many new cardiovascular events.

A strategy using the participant completed questionnaire (Finnish diabetes risk score as an example) as a prestratification tool would also have a relatively low impact on the prevention of cardiovascular disease in a population. As non-responders to cardiovascular risk assessment tend to be less healthy than responders,[41] the real population impact of this approach is likely to be lower than our estimates. The Finnish diabetes risk score questionnaire has not been validated in the UK population and also requires novel data collection.

Compared with the Department of Health recommended screening programme, a similar number of cardiovascular events could be prevented in the UK population with a significantly lower number of adults invited for a vascular risk assessment, through prestratification using routine data. Our sensitivity analysis further suggested that lower attendance rates would result in a narrower gap in benefits between mass screening and stepwise strategies using routine data, which supports the use of routine data as prestratification tools.

It is reassuring that the exclusion of a family history of diabetes, smoking, and body mass index from the Cambridge risk score did not adversely affect the population impact of the strategies incorporating routine data, suggesting that the tool can be used in health systems where data on these variables are not routinely collected. Similarly, the age range invited for screening could be adjusted—for example, from 40-74 years to 50-74 years.

These approaches might reduce the economic costs and the potential psychological harm associated with screening tests.[10] We used the Cambridge diabetes risk score as an example of a simple risk score in a stepwise approach solely for demonstration. Alternative simple versions of existing tools specifically designed to assess cardiovascular risk, such as QRISK,[45] might perform better than a diabetes risk score. However, as with any population based screening strategies based on historical cohort data, the policy would need to be reviewed to keep pace with the changing patterns of risk factors, treatments, and competing risks in the population.

In conclusion, our findings illustrate the potential for using routinely available data for cardiovascular risk stratification before inviting people at high risk to a vascular assessment. Compared with mass screening, this approach may be similarly effective at preventing new cardiovascular events at the population level, with potential cost savings. This approach might also be transferable to resource poor health systems. Although the Finnish diabetes risk score may have a role in

WHAT IS ALREADY KNOWN ON THIS TOPIC

The national screening committee recommends that all adults aged 40-74 who have never been identified through self assessment or record based screening, should be invited for cardiovascular risk assessment

People are required to attend their surgery for biochemical testing

The costs and benefits associated with mass screening for cardiovascular disease are unknown

WHAT THIS STUDY ADDS

Compared with the government recommended mass screening strategy, an approach using routinely available data for cardiovascular risk stratification before inviting people at high risk for a vascular risk assessment may be as effective at preventing new cardiovascular events, with potential cost savings

Similar benefits could also be achieved if vascular risk assessments were limited to adults aged 50 or more

identifying people at risk of undiagnosed or incident diabetes, it cannot be recommended for use to identify those at high cardiovascular risk in the United Kingdom. Further research on the cost effectiveness of different stepwise population based screening strategies is needed to inform future public health policy.

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