ORIGINAL ARTICLE

Which population groups should be targeted for cardiovascular prevention? A modelling study based on the Norwegian Hordaland Health Study (HUSK)

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Abstract

Objective. To assess level of cardiovascular risk factors in a non-selected, middle-aged population. To estimate the proportion target for risk intervention according to present guidelines and according to different cut-off levels for two risk algorithms. **Design.** Population survey, modelling study. **Setting.** The Norwegian Hordaland Health Study (HUSK) 1997–99. **Subjects.** A total of 22 289 persons born in 1950–57. **Main outcome measures.** Own and relatives' cardiovascular morbidity, antihypertensive and lipid-lowering treatment, smoking, blood pressure, cholesterol. Framingham and Systematic Coronary Risk Evaluation (SCORE) algorithms. The European guidelines on CVD prevention in clinical practice were applied to estimate size of risk groups. **Results.** Some 9.7% of men and 7.6% of women had CVD, diabetes mellitus, a high level of one specific risk factor, or received lipid-lowering or antihypertensive treatment. Applying a SCORE (60 years) cut-off level at 5% to the rest of the population selected 52.4% of men and 0.8% of women into a primary prevention group, while a cut-off level at 8% included 22.0% and 0.06% respectively. A cut-off level for the Framingham score (60 years) of 20% selected 43.6% of men and 4.7% of women, while a cut-off level of 25% selected 25.6% of men and 1.8% of women. **Conclusion.** The findings illustrate how choices regarding risk estimation highly affect the size of the target population. Modelling studies are important when preparing guidelines, to address implications for resource allocation and risk of medicalization. The population share to be targeted for primary prevention ought to be estimated, including the impact of various cut-off points for risk algorithms on the size of the risk population.

Key Words: Cardiovascular disease, family practice, guidelines, modelling study, risk

Population-based prevention is the only sustainable strategy for reducing the burden of coronary heart disease [1]. Nevertheless, without targeting individuals at high risk, interventions will have limited impact on the population's CVD morbidity and mortality in short to medium terms [2,3]. Numerous effective interventions are now available, and the idea of the “polypill” illuminates possible future perspectives [4]. A great number of guidelines offer tools for risk assessment, in order to target interventions appropriately [5–9].

Critiques have emerged that present guidelines are too comprehensive because they target a majority of

the population for CVD risk intervention [10,11]. Such guidelines may therefore be experienced as less relevant for clinical practice for reasons of feasibility, and studies have shown clinicians' poor adherence to them [12]. Besides, labelling otherwise healthy people “at risk” may lead to adverse psychological and health outcomes [13], and may imply fundamentally new dilemmas in the field of public health [14].

The purpose of this study was to investigate level and distribution of CVD risk factors in an unselected, middle-aged population and to estimate the proportion targeted for intervention according to

In this study, the European guidelines for CVD prevention in clinical practice classify more than half of men in their forties as the target for primary risk intervention.

- Increasing the cut-off level for the SCORE risk algorithm from 5% to 8% reduces this proportion to 22%, while a cut-off level of 10% includes 11%.
- Modelling studies are important in the preparation phase of new guidelines, to estimate a population group feasible to being targeted, including the impact of various cut-off points for risk algorithms. We also need to address guidelines' impact on resource allocation and possible adverse outcomes of providing drug treatment to large numbers of healthy individuals.

current guidelines. We wanted to illustrate possible ways of adjusting the size of the risk groups, by choosing various cut-off levels of risk algorithms.

Material and methods

The Hordaland Health Study (HUSK)

In 1997–99 a population-based health survey was carried out in Hordaland County in Western Norway: the Hordaland Health Survey (HUSK) [15]. Those invited were a randomly selected sample born in 1950 and 1951 ($n=4849$) and all inhabitants born between 1953 and 1957 ($n=29\,400$). The survey was carried out by the National Health Screening Service, Oslo (now the Norwegian Institute of Public Health) in cooperation with the University of Bergen. Of the 33 549 persons invited, 22 289 (66.6%) responded, 10 249 men (59.1%) and 12 040 women (74.3%) (Table I).

Questionnaire and measurements

Along with an invitation to a health check-up a questionnaire was mailed, addressing smoking, use of antihypertensive or lipid-lowering drugs (LLD), diabetes mellitus and cardio- and cerebrovascular disease (including a family history).

The questionnaires were gathered at the screening station, where systolic (SBP) and diastolic blood pressure (DBP) (average of the last two out of three recordings), as well as height and weight for calculating body mass index (BMI) were recorded, and cholesterol level was measured.

We were thus able to calculate the Framingham [16] and Systematic Coronary Risk Evaluation (SCORE) [17] risk algorithms for all respondents. We extrapolated the values of the two risk scores to the age 60 years.

Guidelines

The European guidelines on cardiovascular disease prevention in clinical practice were used to assess the proportion of the population being targeted for primary or secondary CVD prevention [5]. The guidelines' priorities are shown in Box 1.

Risk algorithms

Risk algorithms are intended for risk stratification for primary prevention of CVD, to identify individuals apparently at low risk but who are actually at high risk. We applied the following scores for risk estimation, both based on gender, age, smoking, SBP, and either total cholesterol or the cholesterol/HDL ratio:

1. The Framingham risk algorithm [16] published in 1991 predicts the 10-year risk for all kinds of coronary events, fatal and non-fatal. A Framingham risk score of $\geq 20\%$ is regarded as high. Until recently, most risk equations have

Box 1. The European guidelines' clinical priority list

The clinical priority list in the European guidelines on cardiovascular disease prevention in clinical practice (pocket version). Individuals who fulfil criteria 1 or 2, or both, are defined as at high risk.

1. Patients with established CHD, peripheral artery disease, and cerebrovascular atherosclerotic disease.
2. Asymptomatic individuals who are at a high risk of developing atherosclerotic cardiovascular disease because of:
 - (a) Multiple risk factors resulting in a 10-year risk of $\geq 5\%$ now (or extrapolated to age 60) for developing a fatal CVD event.
 - (b) Markedly raised levels of single risk factors: cholesterol ≥ 8 mmol/l, LDL-cholesterol ≥ 6 mmol/l, blood pressure $\geq 180/110$ mmHg.
 - (c) Diabetes type 2 and type 1 with micro-albuminuria.
3. Close relatives of:
 - (a) Patients with early onset atherosclerotic CVD
 - (b) Asymptomatic individuals at particularly high risk.
 - (c) Other individuals in routine clinical practice.

Source: De Backer et al. [5]

Table I. Hordaland Health Study (HUSK) 1997–99: Number of persons invited and examined

Year of birth	Males		Females	
	Invited n	Examined n (%)	Invited n	Examined n (%)
1950	1 179	881 (74.7)	1 299	1 067 (82.1)
1951	1 112	783 (70.4)	1 259	1 002 (79.6)
1953	2 974	1 725 (58.0)	2 781	1 982 (71.3)
1954	2 970	1 721 (57.9)	2 845	2 023 (71.1)
1955	3 047	1 703 (55.9)	2 906	2 036 (70.1)
1956	3 034	1 721 (56.7)	2 905	1 996 (68.7)
1957	3 026	1 715 (56.7)	2 912	1 934 (66.7)
Total	17 342	10 249 (59.1)	16 207	12 040 (74.3)

been derived from the Framingham study, but the Framingham equations are found to overpredict coronary events by 57% compared with observed events in a representative sample of British men [17].

- The SCORE (Systematic Coronary Risk Evaluation) system presented in 2003 is based on a pooled dataset of cohort studies from 12 European countries, including Norway [18]. It predicts any kind of fatal CVD event over a 10-year period. The threshold for being at high risk is defined as $\geq 5\%$. The European guidelines on CVD prevention [5] recommend use of the SCORE algorithm, and extrapolation of an individual's risk to the age of 60 when guiding a younger person.

The European guidelines on CVD prevention in clinical practice list close relatives of patients with early onset CVD as a separate risk group (see Box 1). To be able to study risk variations within this group also, we calculated their Framingham and SCORE values and increased them by 50%, according to the observed increase in CVD in this group in the Prospective Cardiovascular Münster (PROCAM) Study [7].

Statistics

Statistical analyses were performed using SPSS version 11. Means and 95% confidence intervals (CI) for the risk scores were calculated for selected groups of the population.

Ethics

The study was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate. Written consent was given by respondents at the screening station.

Results

Table II shows respondents with CVD or specific CVD risk factors and their Framingham and SCORE values.

Table III shows the Framingham and SCORE values, present and extrapolated to age 60 in respondents not assigned to the high-risk group for specific reasons (established disease, single risk factors, or family history of early CVD: 66.7% of men and 67.4% of women). This table also shows the Framingham and SCORE values for persons not assigned to the high-risk group, but who reported

Table II. Hordaland Health Study (HUSK) 1997–99, persons born 1950–57: Risk algorithms applied on population with cardiovascular disease (CVD), CVD risk factors, and antihypertensive or lipid-lowering treatment (n = 10 249 males, 12 040 females).

Risk factors	Males, n (%)	Females, n (%)	Framingham risk score at 60 years mean (95% CI)		SCORE risk score at 60 years mean (95% CI)	
			Males	Females	Males	Females
CVD ¹	116 (1.1)	68 (0.6)	18.0 (16.5 to 19.4)	9.6 (8.2 to 10.8)	5.2 (4.7 to 5.9)	1.4 (1.2 to 1.6)
Diabetes ²	241 (2.4)	330 (2.7)	24.7 (23.1 to 26.4)	16.6 (15.2 to 17.9)	6.2 (5.4 to 7.0)	1.3 (1.2 to 1.5)
Elevated SBP ³	33 (0.3)	35 (0.3)	32.5 (29.4 to 35.5)	17.1 (14.6 to 19.6)	17.7 (15.0 to 20.4)	4.8 (3.9 to 5.7)
Elevated DBP ⁴	38 (0.4)	17 (0.1)	28.6 (25.9 to 31.3)	17.4 (12.9 to 22.0)	12.3 (10.6 to 14.0)	5.3 (3.5 to 7.1)
Elevated chol ⁵	228 (2.2)	141 (1.2)	29.0 (28.0 to 30.1)	16.5 (15.3 to 17.7)	12.5 (11.5 to 13.5)	3.8 (3.3 to 4.3)
Antihypertensives	307 (3.0)	316 (2.6)	20.8 (19.9 to 21.6)	11.5 (10.8 to 12.2)	6.7 (5.9 to 7.4)	1.8 (1.7 to 1.9)
Statins	368 (3.6)	320 (2.7)	17.9 (17.2 to 18.7)	7.9 (7.4 to 8.5)	5.5 (5.2 to 5.8)	1.4 (1.3 to 1.5)

¹Myocardial infarction (71 men, 22 women) or stroke (54 men, 55 women). ²Type 1 or 2. ³ ≥ 180 mm Hg. ⁴ ≥ 110 mm Hg. ⁵ ≥ 8 mmol/l.

Table III. Hordaland Health Study (HUSK) 1997–99, persons born 1950–57. Left column: Risk algorithms for respondents not assigned to the high-risk group for specific reasons¹ (n = 6841 males [66.7% of respondents], 8120 females [67.4% of respondents]). Right column: Risk algorithms for the same respondents, but including persons with early CVD among close relatives² (n = 8897 males [86.8% of respondents], 10 683 females [88.7% of respondents]).

	Not assigned to high-risk group for specific reasons		Including persons with CVD among relatives	
	Males (n = 6841)	Females (n = 8120)	Males (n = 8897)	Females (n = 10 683)
SCORE value at present ³	1.1 (1.1 to 1.1)	0.1 (0.1 to 0.1)	1.2 (1.2 to 1.3)	0.1 (0.1 to 0.1)
SCORE value at 60 years ³	5.4 (5.3 to 5.4)	1.3 (1.3 to 1.3)	6.1 (6.0 to 6.2)	1.5 (1.5 to 1.5)
Framingham value at present ³	8.3 (8.2 to 8.4)	3.0 (2.9 to 3.0)	9.5 (9.4 to 9.6)	3.5 (3.5 to 3.6)
Framingham value at 60 years ³	17.8 (17.6 to 17.9)	7.5 (7.4 to 7.6)	20.2 (20.0 to 19.6)	8.7 (8.6 to 8.8)

¹Without cardiovascular disease or diabetes, with serum cholesterol <8.0 mmol/l, with BP <180/110 mm Hg, without lipid-lowering or antihypertensive treatment, and without early cardiovascular disease in close relatives. ²Risk algorithms are stipulated 50% higher. ³Mean (95% CI).

myocardial infarction before 60 years or apoplexy before 70 years in first-grade relatives, thereby increasing their individual risk scores by 50%.

Table IV shows the Framingham and SCORE values at age 60 for population percentiles of increasing values.

Table V shows the proportion of the population to be targeted for risk intervention, given different cut-off levels of the Framingham or SCORE algorithms. First, 9.7% of men and 7.6% of women will be included in the intervention group on the basis of CVD, diabetes mellitus, high BP or cholesterol levels, or because they are already on CVD drug treatment. Furthermore, by applying a cut-off level of the SCORE algorithm of 5% to the rest of the population, 52.4% of men and 0.8% of women will be included into the group eligible for primary CVD risk prevention. If we choose the SCORE cut-off level at 8%, 22% of men and 0.06% of women will be included, while a cut-off level at 10% includes 10.4% of men and 0.001% of women. For the Framingham algorithm, the recommended cut-off level at 20% includes 43.6% of men and 4.7% of women in the primary prevention group. Cut-off levels at 25% or 30% will include 25.5% or 12.3% of men and 1.8% or 0.005% of women, respectively.

Discussion

Applying the European guidelines on CVD prevention in clinical practice [5] to the fraction of 40- to 49-year-old persons in Western Norway not assigned to the high-risk group for specific reasons revealed that more than half of men were “at risk” and should be targeted for intervention.

The high response rate (66.4%) contributes to strengthen the external validity of our findings. We consider data quality to be good, as only a few questionnaires had to be rejected because of inconsistencies. However, people with poor health, low socioeconomic status, and unhealthy lifestyle are

known to be over-represented among non-respondents in health surveys [19], and unpublished HUSK data reveal that non-participants had lower education and income [20]. We may thus have under-stipulated total risk levels in this population, especially for men, who had a poorer response rate compared with women.

The validity of asking about relatives’ illness and their age when they became diseased can be questioned. In any case, myocardial infarction and stroke are major events in a family’s life, especially when happening before old age. In the Prospective Cardiovascular Münster (PROCAM) Study, a family history of early CVD implied a hazard ratio of having a major coronary event during the 10-year observation period of close to 1.5. On this basis, we chose to increase the Framingham and SCORE values by 50% for the one-quarter who reported myocardial infarction before 60 years or apoplexy before 70 years of age in parents, brothers, or sisters.

CVD incidence and mortality in most industrialized countries are declining [21–23], as are CVD risk factor levels [24]. The Norwegian Institute of Public Health performed population-based studies during the 1970 to 1990s, and found a 15–20% decrease in calculated risk of myocardial infarction during the 22-year registration period [25]. About one in eight of the screened population was given an appointment with a doctor due to high risk – either a high single risk factor or an “Infarction score” above a certain limit. The capacity of GPs for follow-up was stipulated before cut-off levels for intervention were chosen [26]. A Norwegian study using data from a population survey in 2001 found that according to the European guidelines 42% of men aged 45–64 would be candidates for antihypertensive or LLD treatment [11], as compared with 52% in our study population. It is obvious that this large population will be out of reach for primary health-care to handle appropriately according to the guidelines’ recommendations.

Table IV. Hordaland Health Study (HUSK) 1997–99, persons born 1950–57¹ (n = 8897 males, 10 683 females): Percentiles of population with increasing scores of SCORE and Framingham scores at age 60 years.

	Percentiles (% of population)														
	5	10	25	50	75	80	85	90	95	96	97	98	99	99.5	99.9
SCORE 60 years males	2.5	2.9	3.7	5.2	7.6	8.3	9.2	10.6	12.7	13.4	14.5	15.7	17.8	20.2	24.9
SCORE 60 years females	0.6	0.7	0.8	1.2	1.9	2.0	2.3	2.7	3.3	3.5	3.8	4.1	4.8	5.6	7.1
Framingham 60 years males	8.4	10.1	13.4	18.6	25.2	27.3	29.6	32.7	37.7	39.2	41.5	44.5	48.6	53.2	62.3
Framingham 60 years females	2.7	3.3	4.7	7.3	11.2	12.4	14.1	16.1	19.7	21.0	22.4	24.6	27.9	31.0	38.4

¹Without cardiovascular disease or diabetes, with serum cholesterol <8.0 mmol/l, with BP <180/110 mm Hg, and without lipid-lowering or antihypertensive treatment. If early cardiovascular disease in close relatives, risk is stipulated 50% higher.

Table V. Hordaland Health Study (HUSK) 1997–99, persons born 1950–57: Proportion of population eligible for risk intervention by different cut-off levels for SCORE and Framingham risk algorithms¹.

	Men (%) (n = 10 249)	Women (%) (n = 12 040)
Secondary prevention group or single risk factor ²	9.7	7.6
SCORE risk score at age 60 years $\geq 5\%$ ³	52.4	0.8
SCORE risk score at age 60 years $\geq 8\%$ ³	22.0	0.06
SCORE risk score at age 60 years $\geq 10\%$ ³	10.4	0.001
Framingham risk score at age 60 years $\geq 20\%$ ³	43.6	4.7
Framingham risk score at age 60 years $\geq 25\%$ ³	25.6	1.8
Framingham risk score at age 60 years $\geq 30\%$ ³	12.3	0.005

¹If early cardiovascular disease in close relatives, risk is stipulated 50% higher. ²Cardiovascular disease, diabetes mellitus, antihypertensive treatment, statin treatment, SBP = >180 mmHg, DBP = >110 mmHg, or serum cholesterol = >8.0 mmol/l. ³Primary prevention group.

In the SCORE project, the cohorts were selected as typifying high- or low-risk populations, based on cardiovascular death rates standardized for risk-factor levels in study cohorts. The observed fall in CVD risk factors and mortality since these data were collected 30 years ago possibly makes a low-risk computation more suitable for the Norwegian population today, leading to a reduced target population. Elevating the 5% cut-off level of the SCORE risk algorithm would bias in the same direction. For example: a cut-off level of 8% would imply a relative reduction of the male risk group by 58%, as shown in Table V. A cut-off level of 10% would reduce the target population to the level found to be manageable for follow-up in the earlier Norwegian studies [26]. Elevating cut-off level of a certain risk algorithm will lead to fewer false positive and more false negative results when the algorithm is applied in a particular population [18]. On a population level, false positives have an undesirable impact on costs, medicalization, and resource allocation, while it might be argued that in clinical practice false negatives are of greater concern, especially for persons requesting a test [27].

Canadian authors applied six different guidelines on a population sample of men and women aged 20–74 years [28]. They found that the number needed to treat (NNT) in order to prevent one death from CVD varied substantially between the guidelines. Studies show large variations in use of LLD across Europe [29], between Norwegian counties [30], and within selected population [31,32]. Variations in morbidity

may explain only some of the differences [30]. Reimbursement systems, national guidelines, and drug marketing probably play important roles, as do patients' and physicians' attitudes and preferences.

Primary care physicians' "inertia" towards guidelines may reflect uneasiness with the guidelines, because important questions are not being addressed [12]. Therefore, modelling studies are important in the preparation phase of new guidelines, addressing their implications on public health budgets, on private costs, on resource allocation, and not least on their adverse effect on life quality and self-esteem of labelling healthy people as being at risk and in need of drug treatment [13].

Pharmacological CVD risk intervention represents a growing and attractive market for the pharmaceutical industry, implying lifelong treatment for a substantial part of the population [29,33]. Guidelines are meant to assist clinicians' decisions on the basis of current state of evidence regarding whom to treat, and several national expert groups have suggested modifications of risk charts, based on national mortality data [34,35]. However, this issue cannot be handled by medicine alone, but has to include political, economical, and ethical evaluations and choices.

Conflicts of interests

A substantial share of the income of Magne Rekdal's firm Emetra AS comes from projects in cooperation with pharmaceutical firms (Pfizer, GlaxoSmith-Kline, and Astra Zeneca), such as development of electronic tools for calculating cardiovascular risk aimed at general practitioners.

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