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Cardiovascular Risk Estimation and Eligibility for Statins in Primary Prevention Comparing Different Strategies

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Abstract

Recommendations for statin use for primary prevention of coronary heart disease (CHD) are based on estimation of the 10-year CHD risk. It is unclear which risk algorithm and guidelines should be used in European populations. Using data from a population-based study in Switzerland, we first assessed the 10-year CHD risk and the eligibility for statins in 5683 women and men aged 35-75 years without cardiovascular disease, comparing the recommendations by the European Society of Cardiology (ESC) without and with extrapolation of the risk to age 60 years, the International Atherosclerosis Society (IAS) and the US Adult Treatment Panel III (ATP-III). The proportion of participants classified as high-risk for CHD was 12.5% (15.4% with extrapolation), 3.0% and 5.8%, respectively. The proportion of participants eligible for statins was 9.2% (11.6% with extrapolation), 13.7% and 16.7%, respectively. Assuming full compliance to each guidelines, the expected relative reduction in CHD deaths in Switzerland over a 10-year period would be 16.4% (17.5% with extrapolation), 18.7% and 19.3%, respectively; the corresponding number needed to treat to

prevent one CHD death would be 285 (340 with extrapolation), 380 and 440, respectively. In conclusion, the proportion of individuals classified as high-risk for CHD varied over a 5-fold range between recommendations. Following the IAS and the ATP-III recommendations might prevent more CHD deaths at the cost of higher numbers needed to treat compared to ESC guidelines.

Key words: cardiovascular disease, modeling study, risk algorithms, statin prescription guidelines

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Introduction

The primary prevention of cardiovascular disease (CVD) can be achieved through population-based strategies or individualized management of risk factors[1]. The latter require the proper identification of patients at high-risk of CVD for whom treatment –e.g., by lipid lowering drugs- is recommended and for whom a high benefit is expected[2]. Three risk algorithms and corresponding guidelines are used in European countries to help physicians identify patients requiring lipid lowering drugs: the SCORE algorithm[3] of the European Society of Cardiology (ESC)[4], the PROCAM algorithm[5] of the International Atherosclerosis Society (IAS)[6] and the Framingham risk score (FRS) from the U.S. Adult Treatment Panel III (ATP-III)[7]. However, the risk algorithms might not adequately estimate individual risk. For instance, the FRS/ATP-III overestimated coronary heart disease (CHD) risk in several European populations[8]. It remains unclear which risk algorithm and guidelines should be used[9]. Using data from a large population-based study in Switzerland, we compared the proportions of adults classified as high-risk and the proportions eligible for statin treatment following three risk algorithms and guidelines (SCORE/ESC, PROCAM/IAS and FRS/ATP-III). We also estimated the number of CHD events prevented and the corresponding number needed to treat (NNT) to avoid one CHD event over 10 years in the Swiss population aged 35-75 years, if the respective risk algorithm and guidelines were applied.

Methods

Our study was based on the analyses of the data of a cross-sectional, population-based study conducted in Switzerland, the "Cohorte Lausannoise" Study (CoLaus Study)[10,11]. The CoLaus Study was designed to investigate the prevalence and genetic determinants of CVD risk factors in a random sample of all Caucasian adults aged 35-75 years living in the city of Lausanne, Switzerland. The Institutional Review Board in Lausanne approved the protocol. All participants gave written informed consent. From the initial random sample, the participation rate was 41%[10]. Of the 6187 participants of the CoLaus study, we excluded 397 with CVD, defined as self-reported diagnosis of angina, myocardial infarction, stroke, peripheral arterial disease or history of coronary revascularization. A further 107 participants (1.7%) with missing data were also excluded. Thus, the final sample of this analysis consisted of 5683 participants (2621 men and 3062 women).

All participants were interviewed and examined at the Department of Ambulatory Care and Community Medicine in Lausanne between 2003 and 2006. Weight and height were measured and body mass index (BMI) was calculated. After an overnight fast, lipids and glucose were measured as previously described[11]. Blood pressure was measured three times

on the left arm as previously described[12]. The last two blood pressure readings were averaged and considered in the present analysis. Statins and antihypertensive drugs use was assessed after participants brought all current medications, including over-the-counter drugs. Participants were classified as never, former or current smoker based on self-reported smoking habits. Diabetes was defined as self-reported medical diagnosis or using any hypoglycemic medication. Sensitivity analyses using level of blood glucose to define diabetes rather than self-reported diagnosis gave similar risk estimates (data not shown).

We used the PROCAM[5] and the FRS[7] algorithms to estimate the 10-year risk for CHD death and myocardial infarction. According to the ATP-III guidelines[7], high-risk was defined as a CHD risk ≥ 20% (Appendix Table). We used the SCORE algorithm for low risk countries to compute the 10-year fatal CVD risk[3], including a minor correction suggested by one of the authors of the SCORE paper (Fitzgerald AP, personal communication)[13]. The new modified SCORE algorithm is more accurate, yielding modest differences in risk classification when compared to the original risk algorithm (data not shown). In the SCORE/ESC guidelines[4], the high-risk category was defined as a 10-year risk ≥ 5% for fatal CVD, which include CHD, ischemic stroke and peripheral arterial disease. The guidelines also provide a list of medical priorities, including markedly raised levels of single CVD risk factors, and suggest classifying participants with one of these priorities as being high-risk (Appendix Table). Moreover, to better communicate the risk of individuals aged 35 to 60 years, SCORE/ESC guidelines recommend extrapolation of their baseline risks as they were 60 years old[4]. Following the standard procedure for the risk estimation with SCORE/ESC, we modeled the risk in individuals younger than 60 years as if they were 60 years old to generate estimates of the SCORE algorithm with extrapolation. Because the upper age limit of the PROCAM and SCORE algorithms is 65 years, we used the risk prediction of age 65 for participants aged 66 years or older, similar to a previous study[14]. In contrast with FRS/ATP-III and SCORE/ESC, in which patients with diabetes are considered like patients with a previous CHD event, in PROCAM/IAS diabetic patients are incorporated into the risk algorithm and are not directly classified as high-risk. As no PROCAM risk algorithm specific for women was available, we adapted estimates of the PROCAM algorithm for women considering that the absolute CHD risk in non-diabetic women was 4-fold lower compared with men of the same age[5]. A similar 4.5-fold risk difference between gender was found in the German Monica cohort[15]. Consequently, a rough risk prediction for women was done by dividing the risk in men by four for all age categories, except that the risk for diabetic women was considered as equal to the risk for diabetic men of the same age in the PROCAM study[16]. To ensure comparability, identical thresholds to define categories of risk factors were used for each risk algorithm.

We used the most recent guidelines from the ESC[4], IAS[6] and ATP-III[7] with the corresponding algorithm, respectively SCORE[3], PROCAM[5] and FRS[7], to define the LDL levels at which to consider statin treatment (Appendix Table). In general, the vast majority of dyslipidemic patients are treated by statins[17] and only 0.8% of participants in our study were treated by fibrates. Therefore, we did not consider other lipid lowering drugs in this analysis.

The proportions of individuals classified as high-risk and individuals eligible for statins, above those already treated, were assessed according to 10-year age categories and gender. To assess differences between the risk algorithms, we used the assumption that a 10-year risk of fatal CVD ≥ 5% corresponds to a 10-year risk of fatal or non-fatal CHD > 20%[4]. We used Kappa statistics to assess the agreement between guidelines to detect eligible adults for statins. The clinical impact of each risk algorithm/guidelines in the Swiss population aged 35-75 years without CVD was simulated by estimating the number of CHD deaths and first myocardial infarction potentially prevented over 10 years[12] and the number needed to treat (NNT) by 10-year statin treatment to prevent one CHD death or the first myocardial infarction over 10 years, following the methodology proposed by Manuel et al[18]. First, we estimated the

number of eligible persons for statins in the Swiss population aged 35-75 without CVD, applying the results from the CoLaus study to the Swiss population, using data from the Swiss Federal Statistical Office and the 6.4% prevalence of CVD in the CoLaus study[10]. Second, in all age categories, we estimated the effect of increased statin use (from current use to full compliance) on the number of CHD deaths and first myocardial infarction averted using the same success proportion of 29.2% with statins in primary prevention[19]. The efficacy of statins in primary prevention may vary according to various baseline risks and characteristics. Therefore, we assumed a large 95% CI for statin benefit (95% CI: 16.7%-39.8%)[19] that included all relative risks according to various characteristics of participants, such as gender or diabetes[20]. CHD death rates were based on the Swiss Federal Statistical Office, considering that 30% of CHD deaths occur in subject without history of CHD[21]. First myocardial infarction incidence rates in Switzerland were based on local data[22] from the Monica study[15] that were available only for men. Third, using the number of CHD events potentially adverted and the number of eligible for statin treatment in the Swiss population, we estimated the NNT to avoid one CHD event over a 10-year period.

Results

The characteristics of the 2621 men and 3062 women are presented in Table 1. Some 9.7% of men and 7.2% of women reported the prescription of statin. The proportion of hypertensive individuals, diabetics and statin users increased with age, in contrast to current smokers who were more numerous in middle-aged than older-aged categories. The proportion of participants classified as high-risk by sex- and age-categories, according to each risk algorithm, is indicated in Figure 1. Some 18.7% of men were classified as high-risk according to SCORE/ESC (25.0% with extrapolation to age 60), 5.9% according to PROCAM/IAS, and 9.0% according to FRS/ATP-III. Percentages of women classified as high-risk were 7.1% according to SCORE/ESC (7.2% with extrapolation to age 60), 0.5% according to PROCAM/IAS, and 3.1% according to FRS/ATP-III. Differences between scoring systems were particularly important among older adults. A particularly low percentage of women were found to be classified as high-risk with the PROCAM/IAS algorithm, probably related to the rough assumption that the non-diabetic women's risk was 25% of the men's risk, without such data in women older than 65 years. Sensitivity analyses assuming an identical risk in non-diabetic men and women older than 65 years increased modestly the total proportion of women classified as high-risk with the PROCAM/IAS from 0.5% to 1.9% and the total proportion of individuals (women and men) classified as high-risk from 3.0% to 3.7%. For women, the SCORE/ESC with or without extrapolation to age 60 yielded similar risk estimations, as the vast majority of women was classified as high-risk based on the priority list without using the algorithm (data not shown).

The proportions of individuals eligible for statins according to each risk algorithm/guidelines or currently under statin treatment are indicated in Figure 2. The proportions of eligible (and untreated) men were 13.5% according to SCORE/ESC (18.8% with extrapolation to age 60), 19.9% according to PROCAM/IAS and 24.2% according to FRS/ATP-III. The proportions of eligible women were 5.4% according to SCORE/ESC (5.5% with extrapolation to age 60), 8.4% according to PROCAM/IAS and 10.3% according to FRS/ATP-III. With SCORE/ESC, all individuals eligible for statins were among adults classified as high-risk. In contrast, most men for whom statin treatment was recommended according to PROCAM/IAS and FRS/ATP-III were in the intermediate risk category and most women were in the low risk category. Discrepancies in eligibility between guidelines were higher in adults under 65 years (Appendix Figure). Agreement for the eligibility was moderate between SCORE/ESC and

PROCAM/IAS (Kappa =0.43 for men and women) and high between PROCAM/IAS and FRS/ATP-III (Kappa=0.80 for men, 0.88 for women).

The number of first CHD events potentially prevented is indicated in Table 2 and Figure 3. The expected number of CHD deaths in the Swiss population free of CHD aged 35-75 over 10 years was 5540 for men and 1750 for women. The expected number of first myocardial infarction by Swiss men free of CHD aged 35-75 over 10 years was 37 555. For both sexes, the application of SCORE/ESC –assuming full compliance- could potentially reduce 16.4% (95% CI: 9.4%-22.3%) of the 7293 CHD deaths expected over 10 years. Some 17.5% (10.0%-23.9%) would be obtained with the application of SCORE/ESC with extrapolation, 18.7% (10.4%-24.9%) with the application of PROCAM/IAS and up to 19.3% (11.0%-26.3%) with the application of FRS/ATP-III. In men, the proportions of first myocardial infarction averted were similar to the proportions of deaths avoided according to each risk algorithm/guidelines. The greatest difference between statin prescription guidelines in CHD events reduction (CHD deaths or myocardial infarctions) appeared among individuals aged less than 65 years. The estimated NNT to avoid one CHD event with 10-year statin treatment over a 10-year period according to gender- and age-categories using each risk algorithm/guidelines are indicated in Table 2 and Figure 3. The estimated total Swiss population aged 35-75 years without CVD was 1 786 900 for men and 1 835 000 for women. In both sexes, for the prevention of CHD deaths, the lowest NNT 285 (95% CI: 210-500) was obtained applying the SCORE/ESC. The NNT was 340 (250-590) applying SCORE/ESC with extrapolation; 380 (280-670) applying PROCAM/IAS, and 440 (330-780) applying FRS/ATP-III. The estimated NNT to prevent a first myocardial infraction in men ranged from 40 (30-70) applying SCORE/ESC to 60 (40-100) applying FRS/ATP-III (Table 2).

Discussion

In a population-based study in Switzerland, we found that SCORE/ESC classified a greater number of men and women as high-risk than PROCAM/IAS and FRS/ATP-III, especially if they were aged 55 years or more. However, a greater number of participants were eligible for statins applying PROCAM/IAS and FRS/ATP-III compared to SCORE/ESC, especially if they were middle-aged. Whereas ESC guidelines target only individuals classified as high-risk, PROCAM/IAS and FRS/ATP-III guidelines recommend statins also in intermediate and low risk individuals of CHD. As a result, the PROCAM/IAS and FRS/ATP-III strategies could potentially avoid a larger number of CHD events over 10 years in at the cost of a higher NNT compared to SCORE/ESC.

Risk assessment algorithms might not be accurate to properly identify the high-risk individuals due to differences in the prevalence of CVD risk factors between populations. We showed that, when applied to the same population, different risk algorithms used in Europe lead to large differences in CHD risk estimation. Similar to previous reports[23,24], our results confirm the fact that SCORE/ESC classifies as high-risk a large proportion of individuals, particularly from age 55 years onwards. Moreover, the extrapolation of the risk to age 60 years as proposed with SCORE/ESC accentuates the proportion of middle-aged men classified as high-risk. The difference is substantial compared to other guidelines. As the guidelines for drug prescription in primary prevention of CVD base their recommendations on those risk estimations[4,25], the choice of the risk algorithm has major clinical and public health implications.

Following a high-risk strategy, the SCORE/ESC guidelines recommend statins in adults classified as high-risk only[4], while PROCAM/IAS[6] and FRS/ATP-III[7] guidelines also target individuals with intermediate and low CHD risk, depending on their LDL levels. Our results

show that the percentage of participants eligible for statins with the SCORE/ESC high-risk strategy was lower than with the PROCAM/IAS or FRS/ATP–III guidelines, despite the large number of subjects classified as high-risk according to SCORE/ESC. These differences of eligibility between strategies were particularly evident among middle-aged adults, maybe because low risk individuals and young individuals were not eligible for statins according to the SCORE/ESC high-risk strategy. Agreement was good between PROCAM/IAS and FRS/ATP-III; these two guidelines have similar CHD risk and LDL-cholesterol thresholds for statin prescription, except that, with PROCAM/IAS[6], diabetic patients are not directly considered as high-risk in low risk population like Switzerland.

The absolute benefits of a preventive intervention are greater in individuals with a higher CVD risk[2,9] and the vast majority of myocardial infarction appears at advanced age. Therefore, older adults have greater absolute benefits of statins in primary prevention. However, our results show that broader statin prescription strategies such as PROCAM/IAS and FRS/ATP-III could avoid more first CHD events over ten years than high-risk strategies such as SCORE/ESC especially among individuals younger than 65 years. In the Swiss population, a strategy targeting also low risk individuals would prevent more CHD events, because the number of CHD events in relatively young adults is large: 24 780 first myocardial infarctions[22] were reported over the last 10 years among Swiss men aged 35-64 years. However, such a strategy implies the prescription of statins to a large fraction of the population and as a result a high NNT. Moreover, the consequences of prescribing lifelong statins to young individuals are unknown[26]. Previous studies comparing the efficacy of different statin prescription guidelines have shown contradictory results. Because of differences in the methodology and variations in the distribution of risk factors in the populations studied, comparisons with our results are limited: two studies were not population-based[27,28], one studied only men aged 49-65 years and excluded diabetics[29], and another used European guidelines in a North American population[18].

Our study has several limitations. Analyses were based on cross-sectional data from the CoLaus study, yielding only a comparison of individuals' risk estimates. The performance and accuracy of the different algorithms could not be prospectively examined. Because of the modeling design of the study, we used several assumptions to estimate the number of CHD expected and potentially prevented and the NNT. For non-diabetic women aged 35 to 75 years, risk estimation with the PROCAM algorithm was based on a division of the men's risk by 4. This estimation was shown to be valid only for non-diabetic women aged 45 to 65 years[5]. As no PROCAM data are available for women older than 65 years, risk estimates in women older than 65 years with the PROCAM algorithm are uncertain. However, sensitivity analyses considering an equal risk between women and men older than 65 years yielded only modest changes in the proportions of individuals classified as high-risk. Consistency, caution must be observed when interpreting results for individuals aged 65 or more, as SCORE[3] and PROCAM[5] are not validated for adults aged over 65 years. Moreover, outcomes for risk estimation were different according to the algorithm used: SCORE estimates cardiovascular death[3] whereas PROCAM and FRS estimate fatal or non-fatal CHD[5,7]. The choice of the best outcome for risk estimation is still controversial[30] and comparing results of different risk algorithm estimations should be interpreted with caution. The efficacy of statins in primary prevention may vary according to baseline characteristics of participants, such as gender or diabetes, but we used a large 95% CI for statin benefit. Finally, because of the theoretical assumption of full compliance with statin guidelines and the large limits of uncertainty of our results, care should be taken not to over interpret potential differences in the number of events prevented and NNT between guidelines. A unique strength of the study is the use of a large

population-based sample in Switzerland with a standardized and well-described CVD risk factors assessment[10,11].

Conflict of interest statement

Vincent Mooser is a full time employee of GlaxoSmithKline.

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Table 1 : Characteristics of participants.

Age categories, years	**All**	**35-44**	**45-54**	**55-64**	**65-75**
Men	(N = 2621)	(n = 839)	(n = 784)	(n = 650)	(n = 348)
Age (years)	51.8 ± 10.6	40.2 ± 2.7	49.6 ± 2.9	59.9 ± 2.8	69.7 ± 3.1
Body mass index (kg/m^2)	26.4 ± 3.9	25.6 ± 3.6	26.1 ± 3.8	27.3 ± 3.9	27.3 ± 4.0
Systolic BP (mmHg)	131.5 ± 16.3	124.4 ± 11.6	128.9 ± 14.5	137.5 ± 16.9	143.3 ± 18.4
Diastolic BP (mmHg)	81.2 ± 10.7	78.2 ± 9.4	82.0 ± 10.9	83.9 ± 10.6	81.9 ± 11.8
Total cholesterol (mg/dl)	215 ± 39	208 ± 39	219 ± 39	220 ± 38	214 ± 38
HDL-cholesterol (mg/dl)	56 ± 14	55 ± 13	56 ± 14	58 ± 15	58 ± 15
LDL-cholesterol (mg/dl)	133 ± 35	129 ± 35	135 ± 34	135 ± 34	131 ± 34
Triglyceride (mg/dl)	130 ± 70	122 ± 68	137 ± 75	136 ± 69	128 ± 60
Diabetes mellitus	5.7% (149)	1.3% (11)	3.6% (28)	9.8% (64)	13.2% (46)
Current Smokers	29.2% (764)	34.9% (293)	28.2% (221)	28.3% (184)	19.0% (66)
Hypertension treatment	16.3% (428)	4.1% (34)	11.2% (88)	26.6% (173)	38.2% (133)
Statin use	9.7% (255)	3.1% (26)	7.4% (58)	15.2% (99)	20.7% (72)
Women	(N = 3062)	(n = 853)	(n = 877)	(n = 882)	(n = 450)
Age (years)	53.1 ± 10.6	40.2 ± 2.8	49.8 ± 2.9	60.1 ± 2.8	69.9 ± 3.1
Body mass index (kg/m^2)	25.0 ± 4.8	24.0 ± 4.5	24.9 ± 5.0	25.6 ± 5.0	26.0 ± 4.5
Systolic BP (mmHg)	124.4 ± 8.2	114.4 ± 12.2	120.8 ± 15.1	130.1 ± 18.5	139.1 ± 18.7
Diastolic BP (mmHg)	77.5 ± 10.6	74.6 ± 9.7	77.7 ± 0.8	79.7 ± 10.7	78.4 ± 10.1
Total cholesterol (mg/dl)	217 ± 40	195 ± 33	214 ± 38	229 ± 38	238 ± 37
HDL-cholesterol (mg/dl)	70 ± 16	68 ± 14	71 ± 17	71 ± 17	71 ± 17
LDL-cholesterol (mg/dl)	126 ± 36	110 ± 30	124 ± 35	136 ± 35	143 ± 34
Triglyceride (mg/dl)	101 ± 52	86 ± 43	98 ± 54	108 ± 51	121 ± 55
Diabetes mellitus	3.0% (93)	1.6% (14)	2.2% (19)	3.5% (31)	6.4% (29)
Current Smokers	25.2% (773)	28.1% (240)	31.4% (275)	21.8% (192)	14.7% (66)
Hypertension treatment	14.8% (454)	4.0% (34)	9.7% (85)	22.2% (196)	30.9% (139)
Statin use	7.2% (219)	0.9% (8)	3.7% (32)	11.8% (104)	16.7% (75)

Values are reported as mean ± standard deviation or percentage (number). LDL, HDL, and total cholesterol to mmol/l, multiply by 0.0259. Triglycerides to mmol/l, multiply by 0.0113.
Abbreviations: BP: blood pressure. HDL: high-density lipoprotein. LDL: low-density lipoprotein

Table 2. Estimates of potential benefit over 10 years on the Swiss population without cardiovascular disease aged 35-75 years, if different guidelines for 10-year statin treatment were fully implemented.

	Eligible (and untreated) with statins, N [a]	Potential CHD deaths adverted with statins over 10 years, N (95% CI) [b]	Estimated NNT with statins to avoid one CHD death over 10 years, N (95% CI)	Potential first MI averted with statins over 10 years, N (95% CI) [b c]	Estimated NNT with statins to avoid one MI over 10 years, N (95% CI) [c]
Men					
SCORE/ESC	243 720	970 (550-1320)	250 (180-440)	6050 (3460-8250)	40 (30-70)
SCORE/ESC with extrapolation	335 090	1050 (600-1430)	320 (230-560)	7100 (4060-9680)	47 (35-83)
PROCAM/IAS	360 350	1080 (610-1450)	330 (250-590)	7310 (4180-9970)	49 (36-86)
FRS/ATP-III	436 270	1110 (640-1510)	390 (290-690)	7700 (4400-10 500)	57 (41-99)
Women					
SCORE/ESC	96 390	225 (130-310)	430 (310-750)	NA	NA
SCORE/ESC with extrapolation	97 430	230 (130-310)	430 (320-750)	NA	NA
PROCAM/IAS	14 370	280 (150-370)	550 (420-990)	NA	NA
FRS/ATP-III	189 740	300 (170-410)	640 (470-1110)	NA	NA

Abbreviations : ESC, European Society of Cardiology; IAS, International Atherosclerosis Society; FRS/ATP III, Framingham risk score / U.S. National Cholesterol Education Program's Adult Treatment Panel III; 95% CI: 95% confidence interval; CHD, coronary heart disease; MI, myocardial infarction; N, number; NA, not available (see footnotes).

[a] Based on CoLaus and the Swiss Federal Statistical Office data, considering 6.4% as the prevalence of cardiovascular disease in adults aged 35-75 in the CoLaus study[10].

[b] The relative effectiveness of statins in avoiding coronary events was assumed to be 29.2% (95% CI, 16.7- 39.8) for all risk groups in primary prevention, as reported by Thavendiranathan et al[19].

[c] No estimation was available for women, as the Swiss Monica project did not collect outcome data for women[22] and given the lack of other valid prospective data.

Appendix Table. Eligibility criteria for statin treatment according to current risk algorithms and guidelines.

Guidelines	Scoring system	Condition	Eligibility according to lipid levels
ESC 2007	**SCORE**	Diabetes or Priority list [a] or High-risk: 10-year risk for fatal CVD of ≥ 5%	Total cholesterol ≥ 190 mg/dl or LDL ≥ 115 mg/dl
	with extrapolation to age 60 years	Diabetes or Priority list [a] or High-risk if extrapolated to age 60 years	
IAS 2003	**PROCAM** [b]	High-risk : 10-year risk for fatal or non-fatal CHD of >20%	LDL ≥ 100 mg/dl
		Intermediate risk: 10-year risk of 20% - 10%	LDL ≥ 130 mg/dl
		Low risk: 10-year risk < 10% and 2 or more risk factors [c]	LDL ≥ 160 mg/dl
		Very low risk: 10-year risk < 10% and 0 or 1 risk factor [c]	LDL ≥ 190 mg/dl
ATP-III 2001	**FRS**	Diabetes or High-risk: 10-year risk for fatal or non-fatal CHD of >20%	LDL ≥ 100 mg/dl
		Intermediate risk: 10-year risk of 20% - 10%	LDL ≥ 130 mg/dl
		Low risk: 10-year risk < 10% and 2 or more risk factors [c]	LDL ≥ 160 mg/dl
		Very low risk: 10-year risk < 10% and 0 or 1 risk factor [c]	LDL ≥ 190 mg/dl

Abbreviations: ESC, European Society of Cardiology; IAS, International Atherosclerosis Society; ATP-III, U.S. National Cholesterol Education Program's Adult Treatment Panel III; FRS, Framingham Risk Score; CHD, coronary heart disease; CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein. Total and LDL cholesterol to mmol/l, multiply by 0.0259.

[a] Priority list: markedly raised levels of single factors: cholesterol ≥ 320 mg/dl; LDL ≥ 240 mg/dl or blood pressure ≥ 180/110 mm Hg.

[b] Diabetic patients are incorporated into the PROCAM algorithm and not directly classified as high-risk.
[c] Risk factors: current smoking; blood pressure ≥ 140/90 mm Hg or antihypertensive medication; family history of CHD; HDL < 40 mg/dl (HDL ≥ 60 mg/dl counts as a "negative" risk factor); men aged ≥ 45 years; women aged ≥ 55 years.

Figure 1

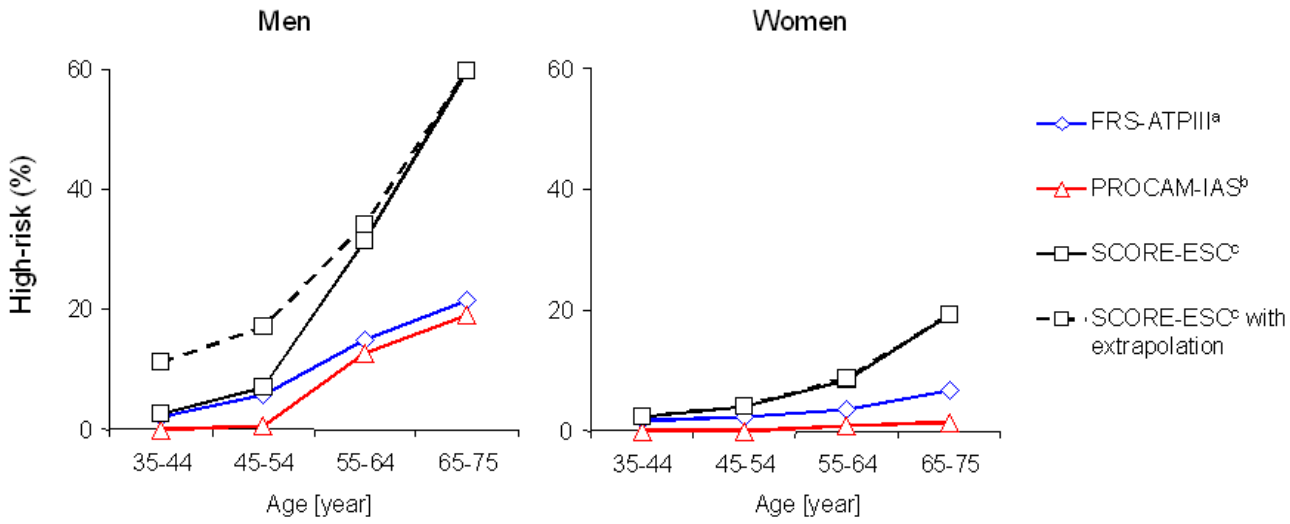


Figure 1 : Percentages of participants at estimated high-risk according to various risk algorithms.
[a] Framingham risk score / U.S. National Cholesterol Education Program's Adult Treatment Panel III; [b]International Atherosclerosis Society; [c]European Society of Cardiology.

Figure 2

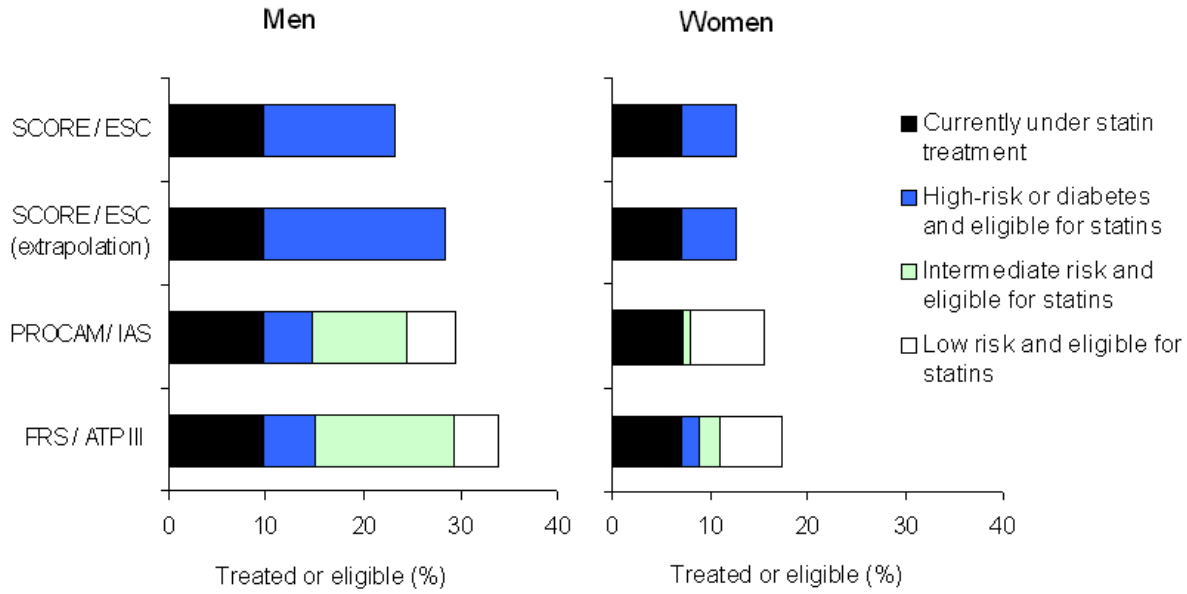
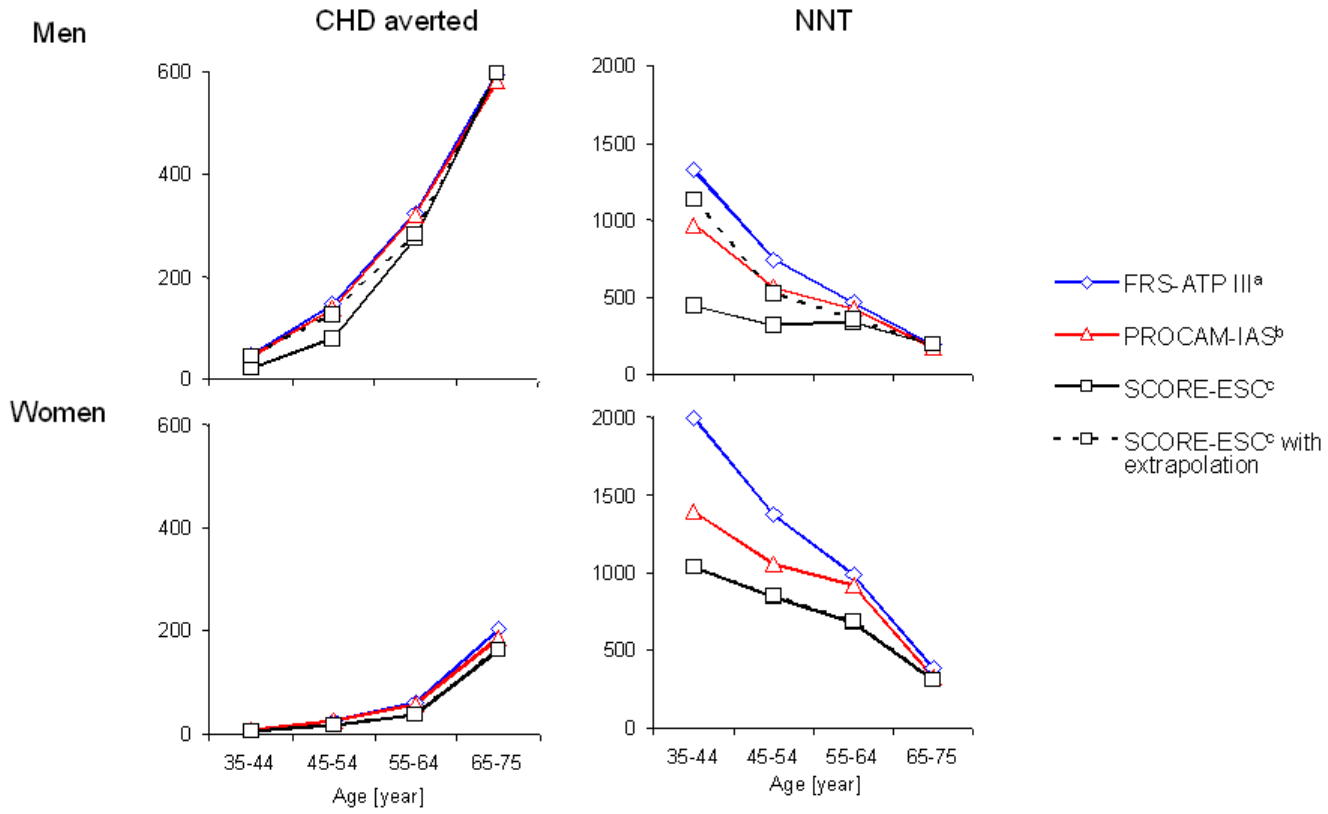


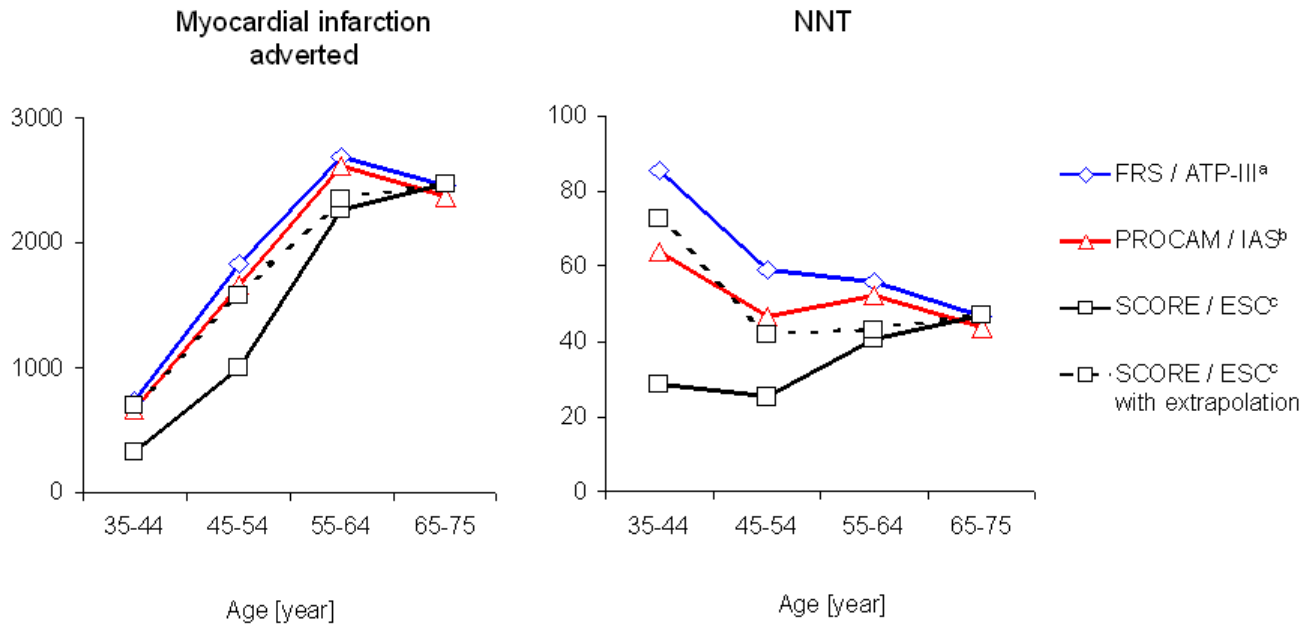
Figure 2 : Percentages of participants currently under statin treatment or eligible according to various strategies.
[a] Framingham risk score / U.S. National Cholesterol Education Program's Adult Treatment Panel III; [b]International Atherosclerosis Society; [c]European Society of Cardiology.

Figure 3
Panel A



Panel A : Estimated number of coronary heart disease (CHD) deaths potentially adverted and number needed to treat (NNT) to avoid one CHD death over 10 years according to different guidelines for 10-year statin treatment, based on a full compliance and extrapolated to the Swiss population without cardiovascular disease aged 35-75 years.

Figure 3
Panel B



Panel B : Estimated number of myocardial infarctions potentially adverted and NNT to avoid one myocardial infarction in a 10-year period with full compliance to different guidelines for 10-year statin treatment, extrapolated to Swiss men without cardiovascular disease aged 35-75 years.
[a] Framingham risk score / U.S. National Cholesterol Education Program's Adult Treatment Panel III; [b]International Atherosclerosis Society; [c]European Society of Cardiology.

Appendix Figure: Percentages of individuals currently under statins or eligible according to different strategies and age.
[a]Framingham risk score / U.S. National Cholesterol Education Program's Adult Treatment Panel III;
[b]International Atherosclerosis Society; [c]European Society of Cardiology.