



Systematic Coronary Risk Evaluation estimated risk and prevalent subclinical atherosclerosis in coronary and carotid arteries: A population-based cohort analysis from the Swedish Cardiopulmonary Bioimage Study

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Background

It is not clear if the European Systematic Coronary Risk Evaluation algorithm is useful for identifying prevalent subclinical atherosclerosis in a population of apparently healthy individuals. Our aim was to explore the association between the risk estimates from Systematic Coronary Risk Evaluation and prevalent subclinical atherosclerosis.

Design

The design of this study was as a cross-sectional analysis from a population-based study cohort.

Methods

From the general population, the Swedish Cardiopulmonary Bioimage Study randomly invited individuals aged 50–64 years and enrolled 13,411 participants mean age 57 (standard deviation 4.3) years; 46% males between November 2013–December 2016. Associations between Systematic Coronary Risk Evaluation risk estimates and coronary artery calcification and plaques in the carotid arteries by using imaging data from a computed tomography of the heart and ultrasonography of the carotid arteries were examined.

Results

Coronary calcification was present in 39.5% and carotid plaque in 56.0%. In men, coronary artery calcium score >0 ranged from 40.7–65.9% and presence of carotid plaques from 54.5% to 72.8% in the age group 50–54 and 60–65 years, respectively. In women, the corresponding difference was from 17.1–38.9% and from 41.0–58.4%. A doubling

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of Systematic Coronary Risk Evaluation was associated with an increased probability to have coronary artery calcium score >0 (odds ratio: 2.18 (95% confidence interval 2.07–2.30)) and to have >1 carotid plaques (1.67 (1.61–1.74)).

Conclusion

Systematic Coronary Risk Evaluation estimated risk is associated with prevalent subclinical atherosclerosis in two major vascular beds in a general population sample without established cardiovascular disease or diabetes mellitus. Thus, the Systematic Coronary Risk Evaluation risk chart may be of use for estimating the risk of subclinical atherosclerosis.

Keywords

Systematic Coronary Risk Evaluation • estimated risk • subclinical • atherosclerosis • population

Introduction

The mortality from coronary artery disease is declining in developed countries, but cardiovascular disease is still a leading cause of mortality and morbidity.¹ Although there is overwhelming evidence that effective risk factor management reduces the risk of cardiovascular events, there is an urgency to improve the implementation of prevention guidelines.²

European guidelines recommend using the Systematic Coronary Risk Evaluation (SCORE) charts to assess patients' overall cardiovascular risk in order to guide risk factor treatment.³ The SCORE algorithm estimates the 10-year absolute risk of a fatal cardiovascular event and is based on age, sex, smoking, systolic blood pressure and total cholesterol. An updated SCORE algorithm for Sweden was recently shown to more adequately predict the number of cardiovascular deaths compared with the previous version.⁴ In addition to the 10-year absolute risk of a fatal cardiovascular event, information about the probability that an atherosclerotic disease is already present may increase the awareness of risk and thereby improve the patient's motivation and call for specific secondary prevention measures.⁵ However, it is not clear if the SCORE algorithm is useful for identifying subclinical atherosclerosis in a population of apparently healthy individuals and there are, so far, no SCORE charts indicating the risk of prevalent subclinical atherosclerosis.

We hypothesised that the SCORE algorithm can be useful also for estimating the risk of prevalent subclinical atherosclerosis in individuals without established cardiovascular disease or diabetes mellitus. Accordingly, our aim was to explore the associations between the risk estimates from the SCORE algorithm and the risk of prevalent subclinical atherosclerosis defined as presence of atherosclerosis in the coronary and carotid arteries. We also wanted to generate new SCORE charts that can be used in individual consultations. For these purposes, we used a recent large population survey in Sweden, the Swedish Cardiopulmonary Bioimage Study (SCAPIS).

Methods

SCAPIS

SCAPIS is a collaborative project between six Swedish universities, aiming to randomly invite 30,000 individuals from the general population living in six Swedish university cities (Gothenburg, Linköping, Malmö/Lund, Stockholm, Umeå and Uppsala), aged 50–64 years. The overall participation rate in SCAPIS was 50%. In addition to determining the traditional cardiovascular risk factors, the participants underwent extensive imaging,

including non-contrast and contrast-enhanced computed tomography (CT) coronary angiography; CT scanning of the abdomen for the quantification of visceral and subcutaneous adipose tissue, liver fat; and ultrasound analysis for carotid artery atherosclerosis.⁶ The study was approved by the Umeå Ethical Review Board (# 2010-228-31 M), and all participants provided written informed consent.

Study population

Of the 15,810 participants enrolled in the SCAPIS cohort between November 2013–December 2016, 13,411 participants were included in the analysis after excluding participants with; prevalent cardiovascular disease or diabetes mellitus and missing data ($n = 1578$ and 821 , respectively) (Figure 1). In addition to assessing the traditional cardiovascular risk factors, we recorded data from a computed tomography scan of the heart and ultrasonography of the carotid arteries. We analysed coronary artery calcium score as present or absent coronary calcification and presence of plaques in any of the carotid arteries.

SCORE

The 2015 SCORE Sweden Risk Chart was used⁴ to calculate a score for each participant. This requires data on sex, age, smoking, systolic blood pressure and total cholesterol. Current smoking status was collected from a questionnaire. Systolic blood pressure was measured in the supine position twice in each arm with an automatic device (Omron M10-IT. Omron Health Care Co., Kyoto, Japan) using the mean systolic blood

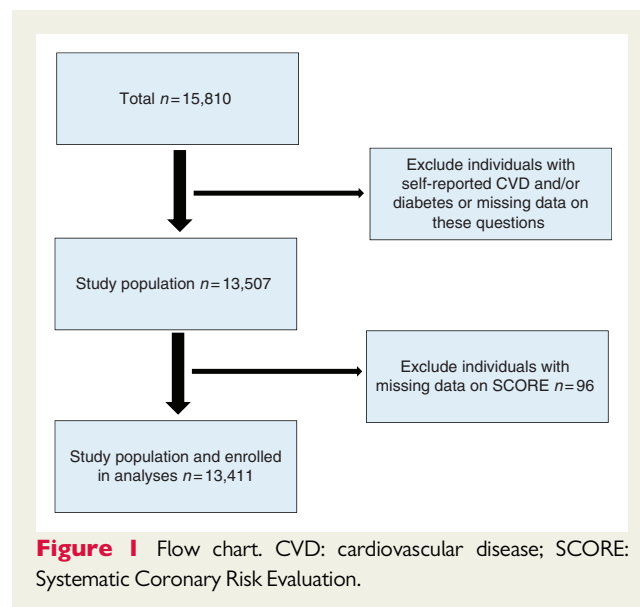


Figure 1 Flow chart. CVD: cardiovascular disease; SCORE: Systematic Coronary Risk Evaluation.

pressure from the arm with the highest mean. Total cholesterol was analysed at the respective university hospital laboratory using a venous blood sample collected after an overnight fast. Based on the calculated SCORE, and presence of certain single risk factors (see below), each participant was assigned to one of four risk groups (low risk <1%, moderate risk 1–4%, high risk 5–9% or very high risk \geq 10%).

Coronary artery calcification

Coronary artery calcification was assessed in non-contrast enhanced images from a state-of-the-art multi-slice computed tomography scanner (Siemens, Somatom Definition Flash, Siemens Healthineers, Erlangen, Germany). Imaging and analyses were performed using a calcium scoring protocol and the calcium content in each coronary artery was measured and summed to produce a total coronary artery calcification score (CACs) according to international standards.^{7,8} An Agatston score >0 was defined as having coronary artery calcification.

Carotid artery plaque

Atherosclerosis in the carotid arteries was determined by using a standardized protocol with a Siemens Acuson S2000 ultrasound scanner equipped with a 9L4 linear transducer (both from Siemens Healthineers, Erlangen, Germany). The left and right carotid artery were insonated and atherosclerotic plaques in the common carotid artery, bulb or in the internal carotid artery fulfilling the Mannheim consensus⁹ were identified. Accordingly, plaques were defined as focal structures encroaching into the arterial lumen of at least 0.5 mm or 50% of the surrounding Intima media thickness (IMT) value, or demonstrates a thickness >1.5 mm as measured from the intima-lumen interface to the media-adventitia interface. Visually detected plaques in the carotid arteries, were summed as a number of total plaques value. Significant carotid atherosclerosis was defined by >1 plaque in the carotid arteries.

Statistics

The study population was described with total number and percentage, mean and 95% confidence interval (CI) or median and interquartile range (IQR). Chi-square, analysis of variance (ANOVA) and the Kruskal-Wallis test were used for analysing group differences.

As noted by others, the SCORE distribution is highly positively skewed in middle-aged population cohorts. CACS is commonly analysed as a categorical variable due to its known skewed distribution with a large proportion of zeros. A similar skewed distribution was noted for carotid plaque burden in this population, also with an excessive number of zeros. To meet the assumption of a linear relationship between the log odds and SCORE we used the log₂ transformation of SCORE to investigate the association between SCORE and CACS and between SCORE and plaque burden using both logistic and nominal regression analyses. CACS was for the logistic regression analysis categorised into CACS < 100 vs CACS \geq 100, while four categories commonly used in clinical praxis, were applied in the nominal regression model; 0, 1–99, 100–399, and \geq 400. Carotid plaque burden was dichotomised into having no significant carotid atherosclerosis (\leq 1 plaque) vs having significant carotid atherosclerosis (>1 plaques) in at least one side of the carotid arteries for the logistic regression analysis, and into three categories for the nominal regression analysis; \leq 1 plaque, >1 plaques in one of the carotid arteries, and >1 plaques in both sides of the carotid arteries. The C statistic was calculated for the logistic regression models.

Zero-inflated negative binomial regression technique has previously been suggested for analysing CACS, as it compensates for the excessive numbers of zeros in the dependent variable.¹⁰ The model consists of two separate models. One model, a logit model, predicted whether an individual has a zero value or not. The second model, a negative binomial

model predicted the value for participants who are not certain zeros. Finally, the two models were combined. In these models, CACS and also plaque burden were used as continuous variables and SCORE was used without transformation. Results of the zero-inflated models are given as [Supplementary Material](#) data. The results from the analyses are presented with odds ratios and 95% CIs.

Risk charts, corresponding to the SCORE chart, were generated for the probability of having CACS \geq 100 and >1 plaques in at least one side of the carotid arteries, respectively. A logistic regression model was applied to estimate the probabilities based on sex, age, smoking, total cholesterol and systolic blood pressure and separate models for women and men were applied.

SPSS version 24 and R version 3.2.0 were used to perform the analyses.

Results

Coronary calcification was present in 39.5% and plaques in any of the carotid arteries in 56.0% of the participants. Baseline characteristics in different categories of CACS and plaque burden in the carotid arteries are shown in [Table 1](#). The distribution of CACS >0 and CACS \geq 100 and atherosclerosis in the carotid arteries in relation to sex and age is shown in [Figure 2\(a\)–\(d\)](#) and in different SCORE categories is further illustrated in [Figure 3\(a\)](#) and (b), respectively.

SCORE related to CACS

In a logistic model, a doubling of SCORE was associated with an increased probability to have CACS >0 as compared to CACS = 0, odds ratio (OR) 2.18 (95% CI, 2.07–2.30), Wald $\chi^2(1) = 850$, $p < 0.001$, C statistic 0.75 (95% CI, 0.74–0.76). In an ordinal model, a doubling of SCORE was associated with an increased probability of being in a higher CACS category, OR 2.04 (95% CI, 1.97–2.10), Wald $\chi^2(1) = 1840$, $p < 0.001$. There was a higher proportion of antihypertensive or/and lipid lowering agent users with increasing CACS ([Supplementary Material, Table S1](#)). Sensitivity analysis showed that the association between a doubling of SCORE and the probability to have CACS >0 as compared to CACS = 0 remained basically unchanged after excluding participants on antihypertensive ($n = 2420$) or/and lipid lowering ($n = 941$) agents, OR 2.17 (95% CI, 2.04–2.31), Wald $\chi^2(1) = 595$, $p < 0.001$. The zero-inflated models confirmed the association between SCORE and CACS ([Supplementary Material](#)). Data on sensitivity, specificity, positive and negative predictive values for different SCORE-levels are given as [Supplementary Material Table S2\(a\)](#) and (b). A SCORE < 1 could exclude CACS \geq 100 with a negative predictive value of 98% and a SCORE \geq 5 could detect CACS \geq 100 with a positive predictive value of 32%.

SCORE related to plaque in the carotid arteries

In a logistic model, a doubling of SCORE was associated with an increased probability to have >1 plaques in any of the carotid arteries, OR 1.67 (95% CI, 1.61–1.74), Wald $\chi^2(1) = 647$, $p < 0.001$. In an ordinal model, a doubling of SCORE was associated with an increased probability of being in a higher carotid plaque category, OR 1.69 (95% CI, 1.63–1.76), Wald $\chi^2(1) = 683$, $p < 0.001$, C statistic 0.67 (95% CI, 0.66–0.68). There was a higher proportion of antihypertensive or/and lipid lowering agent users with increasing carotid plaques

Table 1 Overview of baseline characteristics in different categories of subclinical atherosclerosis. The Swedish Cardiopulmonary Bioimage Study (SCAPIS), 2013–2016.

Total	CACs ^a					Carotid plaque category ^a			p
	0	1–99	100–399	≥400	p	≤1 plaque	>1 plaque	Plaques	
						one side	both sides		
n	7971 (60.5%)	3740 (28.4%)	1061 (8.0%)	409 (3.1%)	<0.001	11010 (82.3%)	1797 (13.4%)	575 (4.3%)	<0.001
Sex (men)	35.5%	58.6%	69.6%	79.5%		43.5%	55.9%	64.5%	
Age	57.4 (57.3–57.4)	58.1 (58.0–58.2)	59.1 (58.9–59.4)	60.1 (59.8–60.5)		57.1 (57.0–57.2)	58.5 (58.3–58.7)	59.3 (59.0–59.7)	
Smoking status					<0.001				
Never smoker	52.8%	44.3%	36.8%	33.7%		50.6%	40.2%	34.5%	
Ex-smoker	35.6%	40.1%	44.0%	43.8%		37.1%	40.9%	41.6%	
Current smoker	11.7%	15.5%	19.2%	22.5%		12.2%	18.9%	23.9%	
Unknown (1.0%)									
Systolic BP	124.8 (124.5–125.1)	127.9 (127.3–128.4)	130.8 (129.8–131.8)	133.5 (131.9–135.2)	<0.001	123.7 (123.3–124.0)	129.3 (128.4–130.1)	133.4 (132.0–134.9)	<0.001
Diastolic BP	76.3 (76.2–76.5)	77.8 (77.5–78.2)	78.9 (78.3–79.6)	79.6 (78.6–80.6)	<0.001	75.9 (75.7–76.1)	77.9 (77.4–78.3)	79.0 (78.1–79.9)	<0.001
Total cholesterol	5.6 (5.5–5.6)	5.6 (5.6–5.7)	5.7 (5.6–5.7)	5.5 (5.4–5.6)	<0.001	5.5 (5.5–5.6)	5.7 (5.6–5.7)	5.7 (5.7–5.8)	<0.001
SCORE ^b	0.9 (0.5–1.7)	1.2 (0.7–2.0)	1.7 (1.0–2.6)	2.2 (1.4–3.2)	<0.001	0.8 (0.5–1.5)	1.3 (0.7–2.3)	1.7 (1.0–2.8)	<0.001
SCORE Class					<0.001				
Low risk	34.4%	12.8%	5.9%	2.7%		27.9%	13.5%	5.9%	
Moderate risk	64.4%	83.7%	88.3%	86.1%		70.4%	81.1%	84.0%	
High risk	1.1%	3.2%	5.4%	10.8%		1.6%	4.7%	9.6%	
Very high risk	0.2%	0.3%	0.4%	0.5%		0.1%	0.6%	0.5%	

BP: blood pressure; CACS: coronary artery calcium score; CI: confidence interval; IQR: interquartile range; SCORE: Systematic Coronary Risk Evaluation.

Data presented as proportions, mean (95% CI) or median (IQR).

^aMissing data are excluded, n=230 for CACS and n=29 for carotid plaque category.^bMedian and Q1–Q3.

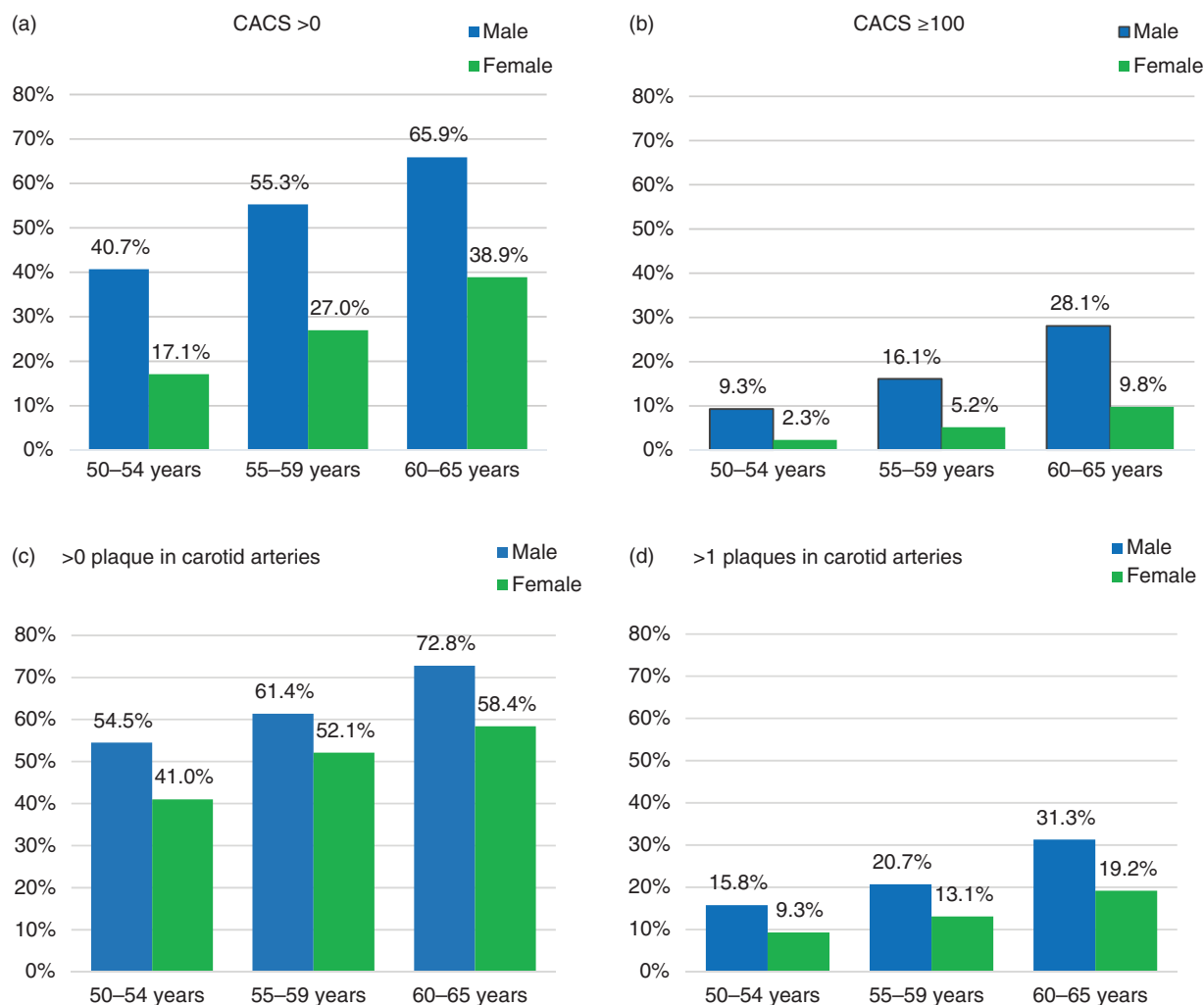


Figure 2 Prevalence of coronary artery calcium score (CACS) > 0 ($n = 5210$), CACS ≥ 100 ($n = 1470$), plaque in any carotid artery ($n = 7498$) and > 1 plaques in any carotid artery ($n = 2372$) by age and sex.

(Supplementary Material Table S1). In a sensitive analysis, where participants who reported using antihypertensive or/and lipid lowering agents were excluded, a doubling of SCORE was still associated with OR 1.66 (95% CI, 1.58–1.74), Wald $\chi^2(1) = 475$, $p < 0.001$ for having > 1 plaques in any of the carotid arteries. The zero-inflated models confirmed the association between SCORE and carotid plaques (Supplementary Material). Data on sensitivity, specificity, positive and negative predictive value for different SCORE-levels are given as Supplementary Material Table S2(a) and (b). A SCORE < 1 could exclude more than one carotid plaque with a negative predictive value of 92% and a SCORE ≥ 5 could detect more than one carotid plaque with a positive predictive value of 45%.

Prevalence of atherosclerosis in coronary and carotid arteries

The prevalence of subclinical atherosclerosis in coronary and carotid arteries is graphically illustrated in Figure 4(a)–(d) showing the

estimated prevalence of CACS ≥ 100 and > 1 plaques in carotid arteries, respectively, stratified for; sex, age, systolic blood pressure, total cholesterol and smoking. The SCORE risk charts were useful to identify patients from low to a very high risk of having atherosclerosis.

Discussion

This is the first analysis from the SCAPIS, which is so far the largest study in which a random sample from the general population has been examined for presence of both coronary artery calcification and carotid plaques. In the present analysis, including 13,411 participants, SCORE estimated risk was strongly associated with prevalent subclinical atherosclerosis in two major vascular beds in a general population sample without established cardiovascular disease or diabetes mellitus. The analysis also shows that the SCORE risk charts were able to stratify individuals from those

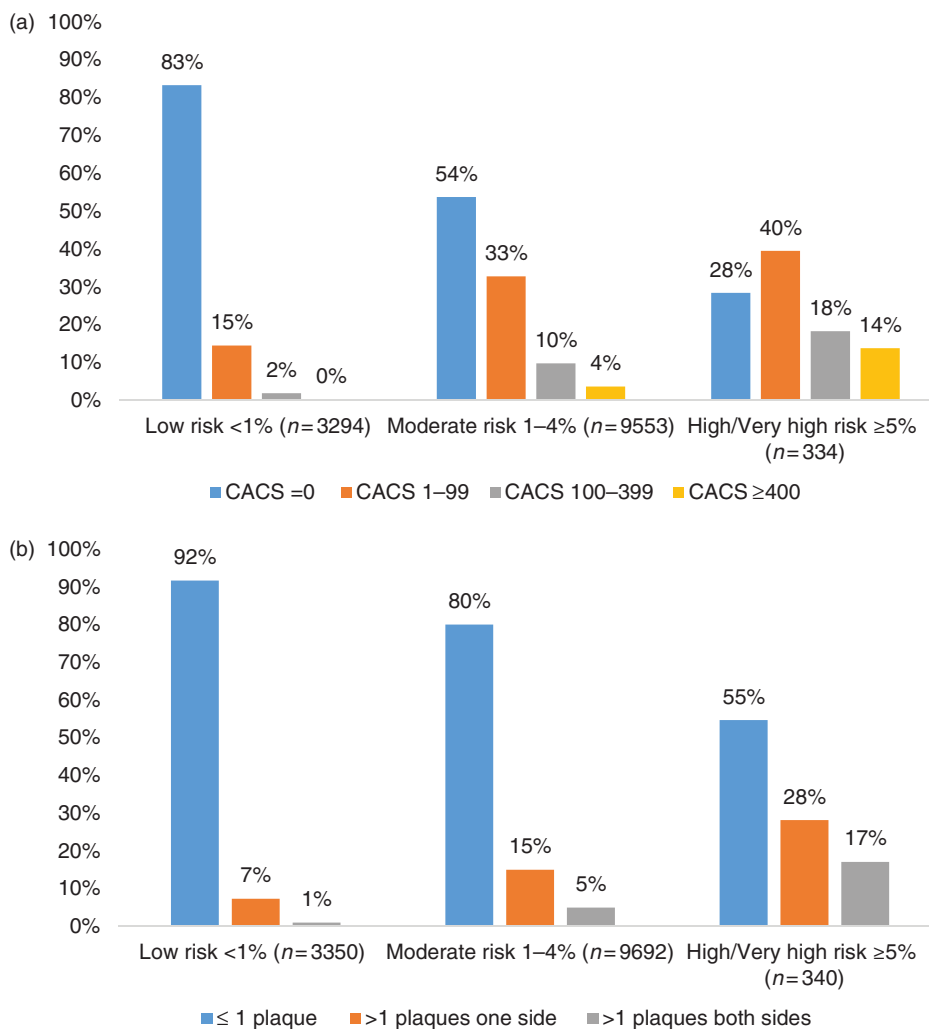


Figure 3 (a) Systematic Coronary Risk Evaluation (SCORE) in three risk category groups by four groups of coronary artery calcium score (CACS). (b) SCORE in three category groups by three groups of carotid plaque.

with low risk to those with very high risk of having subclinical atherosclerosis. A SCORE < 1 indicated a low risk of significant coronary or carotid artery disease, with a negative predictive value of 92–98%, whereas a SCORE ≥ 5 indicated a high risk, with a positive predictive value of 32–45%.

Strengths and limitations of this study

The major strength of the present population-based study is the sample size of more than 13,000 randomly selected individuals examined according to a common, standardised and detailed protocol. Still, the study confers a risk of selection bias, and because of the observational nature we cannot determine causality. Regarding potential selection bias we know from the pilot study that low socio-economic status was associated with lower participation rate.¹¹ Furthermore, we observed an association between living in a low-socioeconomic status area and elevated coronary artery calcification.¹² However, this bias would most likely confer an underestimation of the relationship between SCORE and subclinical atherosclerosis in our study. CACS

was used as a marker of subclinical atherosclerosis in the coronary arteries and is recommended by clinical guidelines in Europe³ in selected asymptomatic individuals. Calcification is associated with the extent of total coronary plaque burden^{13,14} but coronary artery calcification is not an indicator of the (in)stability of an atherosclerotic plaque¹⁵ and absence of calcification does not exclude presence of non-calcified plaques, which may be a limitation. If the non-calcified plaques could also have been identified (increasing the pre-test likelihood), this would have resulted in higher positive predictive values. Finally, the study included participants in one country who were mainly from European origin. Thus, our findings may not be generalisable to other populations.

Comparison with other studies

The association between future risk for cardiovascular disease and CACS has already been well established.^{16,17} Our findings are in accordance with a smaller study published in 2011 from the Multi-Ethnic Study of Atherosclerosis (MESA) showing a strong association

between the estimated 10-year Framingham Risk Score and CACS in 5660 individuals between 45–84 years of age.¹⁸ For each increase of 5% in the 10-year risk for coronary heart disease events using the Framingham Risk Score, the odds of having a positive CACS nearly doubled.¹⁹ Also, in the Progression of Early Subclinical Atherosclerosis (PESA) study, including 4066 bank employees

between 40–54 years of age, the prevalence of subclinical atherosclerosis was higher in those with higher Framingham 10-year risk score.²⁰ In that study, 58% of those at low risk according to SCORE had signs of subclinical atherosclerosis defined as CACS > 0, or plaques detected in the carotids, abdominal aorta or iliofemoral territories, compared with 90% in those with at least a moderate risk. In our

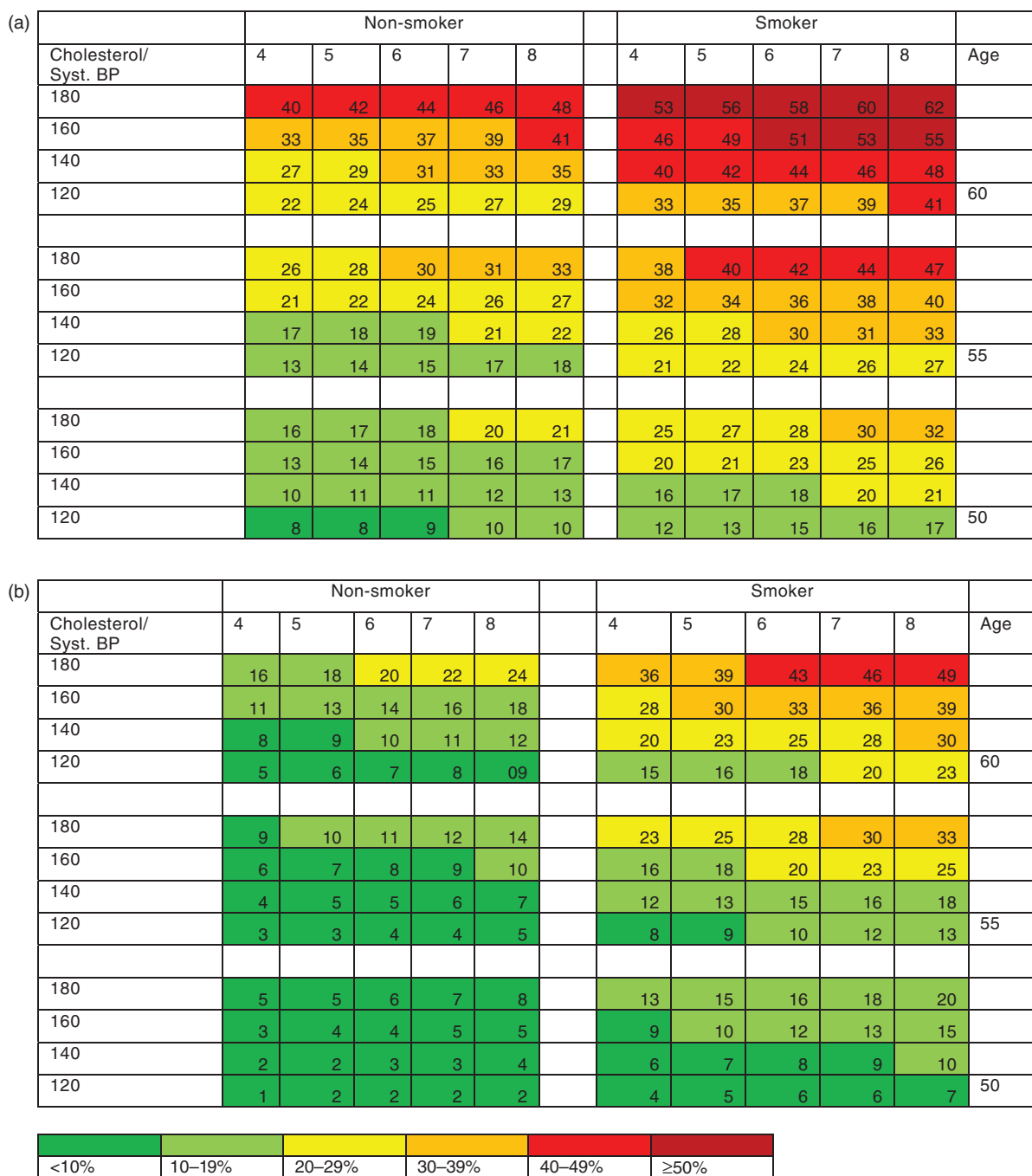


Figure 4 (a) Estimated proportion (%) of men with coronary artery calcium score (CACS) ≥ 100 stratified by age, blood pressure (BP), cholesterol and smoking. (b) Estimated proportion (%) of women with CACS ≥ 100 stratified by age, BP, cholesterol and smoking. (c) Estimated proportion (%) of men with >1 carotid plaque in any carotid artery stratified by age, BP, cholesterol and smoking. (d) Estimated proportion (%) of women with >1 carotid plaque in any carotid artery stratified by age, BP, cholesterol and smoking.

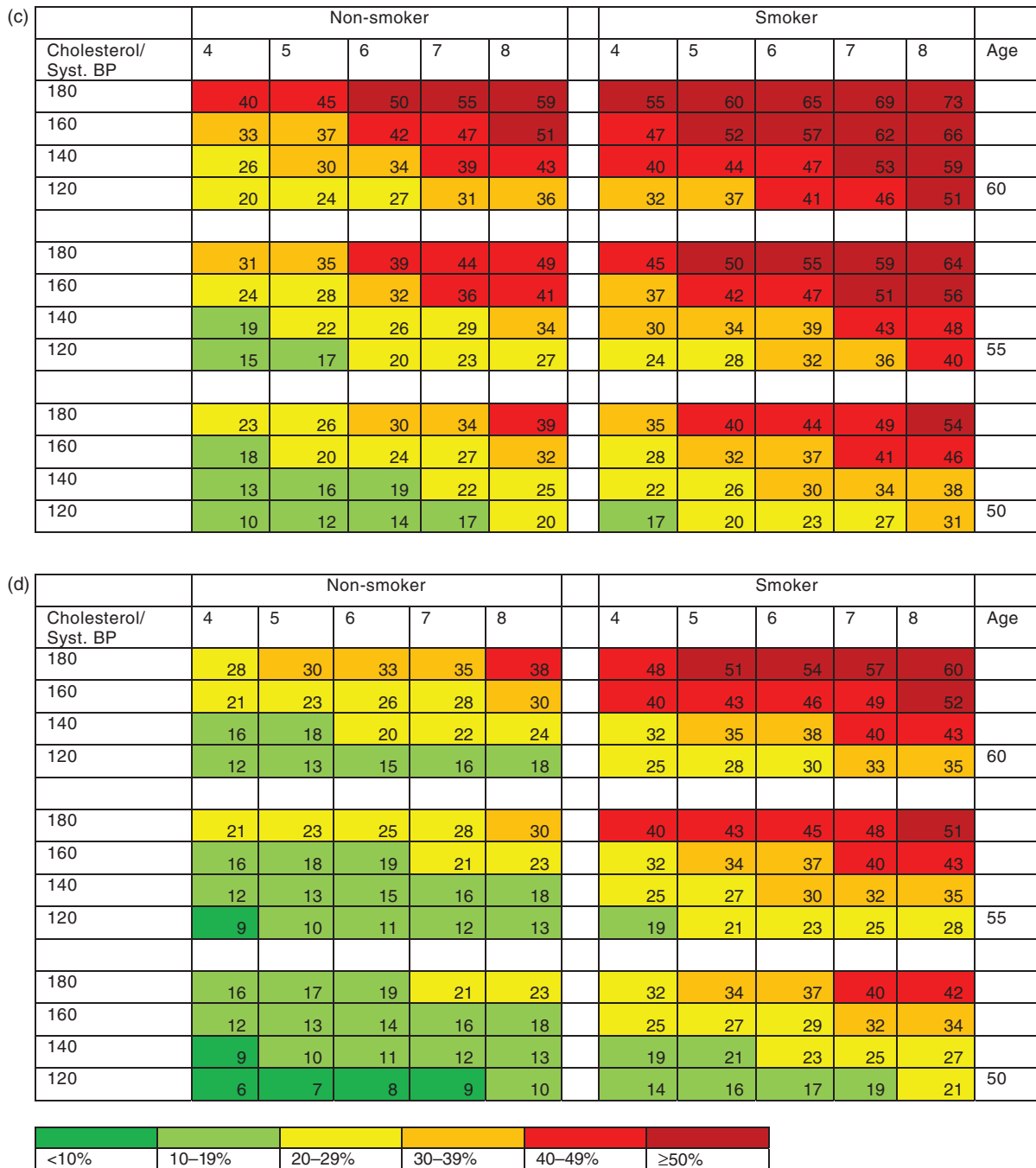


Figure 4 Continued.

study, the majority of subjects were in the moderate SCORE risk group. Interestingly, a previous study in the field on a predominantly low-risk group without cardiovascular disease found that current decision thresholds using SCORE had a very low sensitivity, especially in women, to detect increased vascular ageing.²¹ We have used visually detected plaques in the carotid arteries according to the Mannheim consensus⁹ as a measure of carotid atherosclerosis in this study. However, other studies in the field have used total plaque area in mm².²²

The novelty of our study is that it explores the association between SCORE and subclinical vascular disease by measuring both coronary artery calcification and atherosclerotic plaques in the carotid arteries in a large random contemporary sample of the general population. In this aspect, the results from our study fill a gap of knowledge. The age distribution pattern, illustrated in Figure 2(a)–(d), of prevalent subclinical atherosclerosis is overall similar in carotid and coronary arteries, however, with differences between men and women. The degree of association between

coronary and carotid atherosclerosis remains an unsolved issue that remains to be scrutinised in future publications.

Clinical implications

Most guidelines recommend a mixture of opportunistic and systematic screening.^{3,23} In Europe, the SCORE charts are recommended in apparently healthy people and not for those with established cardiovascular disease or at high risk for other reasons such as type 2 diabetes or chronic kidney disease. In many countries, the general practitioners have a unique role in identifying individuals at risk but without established cardiovascular disease and assessing their eligibility for preventive intervention that may include lifestyle changes and pharmaceutical treatment.

What is the clinical relevance of knowing whether an individual has a high probability of having subclinical atherosclerosis? Firstly, most cardiovascular risk factor management guidelines do not advocate the use of coronary or carotid imaging to detect subclinical atherosclerosis for treatment decisions. However, the finding that a doubling of SCORE was associated with a doubling of the odds for having significant subclinical calcification in the coronary arteries and almost a doubling of the odds for having carotid plaques is easy to remember as a rule of thumb applicable in clinical practice. Secondly, and maybe more importantly, the final decision regarding preventive treatment is made by the physician together with the patient, where the patient's perception of risk is important. This was recently illustrated in a randomised clinical trial where ultrasound-based pictorial information targeting both primary care physicians and individuals, reduced the cardiovascular disease risk factor burden after one year.²⁴ Accordingly, the perception of the link between the patient's modifiable risk factors, such as smoking, lipids and blood pressure and subclinical atherosclerosis may be enhanced by using the charts illustrated in [Figure 4\(a\)–\(d\)](#) and, thus, may be helpful to motivate the patient to adhere to lifestyle changes and pharmaceutical treatment. Thirdly, future studies may demonstrate detection of subclinical atherosclerosis by imaging to be beneficial in primary prevention. This will increase the importance of identifying individuals who will have a high probability of a positive imaging test result.

Conclusions

In summary, subclinical atherosclerosis in the coronary and carotid arteries was highly prevalent in this middle-aged cohort without established cardiovascular disease or diabetes mellitus. The SCORE estimated risk proved, beyond predicting the 10-year absolute risk of a fatal atherosclerotic event, to also be a potentially clinically useful tool for evaluating the risk for having prevalent subclinical atherosclerosis. The risk charts visualising the link between patient's modifiable risk factors and the risk of having subclinical atherosclerosis may also be relevant to motivate the patient to adhere to suggested lifestyle changes and pharmaceutical treatment.

Supplemental material

[Supplementary material](#) is available at *European Journal of Preventive Cardiology* online.

Author contribution

CJÖ, TJ, OA, KC, ME, EF, EH, MM, UN, EO, AP, JP, ES, KF, SS, GB, AB, JB GE, DE, LL, JO, MP, AR, JS and JEE contributed to the to the conception, design and data interpretation of the work. CJÖ, TJ, OA, KC, ME, EF, EH, MM, UN, EO, AP, JP, ES and KF contributed to the acquisition or analysis of data for the work. CJÖ and TJ drafted the manuscript. All revised the manuscript, gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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References

- Nichols M, Townsend N, Scarborough P, et al. Trends in age-specific coronary heart disease mortality in the European Union over three decades: 1980-2009. *Eur Heart J* 2013;**34**:3017–3027.
- Kotseva K, De Bacquer D, De Backer G, et al. Lifestyle and risk factor management in people at high risk of cardiovascular disease. A report from the European Society of Cardiology European Action on Secondary and Primary Prevention by Intervention to Reduce Events (EUROASPIRE) IV cross-sectional survey in 14 European regions. *Eur J Prev Cardiol* 2016;**23**:2007–2018.
- Piepoli MF, Hoes AW, Agewall S, et al. 2016 European guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) developed with the special contribution of the European Association for Cardiovascular Prevention and Rehabilitation (EACPR). *Eur Heart J* 2016;**37**:2315–2381.
- Karjalainen T, Adiels M, Björck L, et al. An evaluation of the performance of SCORE Sweden 2015 in estimating cardiovascular risk: The Northern Sweden MONICA Study 1999–2014. *Eur J Prev Cardiol* 2017;**24**:103–110.
- Mamudu HM, Paul TK, Veeranki SP, et al. The effects of coronary artery calcium screening on behavioral modification, risk perception, and medication adherence among asymptomatic adults: A systematic review. *Atherosclerosis* 2014;**236**:338–350.
- Bergström G, Berglund G, Blomberg A, et al. The Swedish CardioPulmonary BioImage Study: Objectives and design. *J Intern Med* 2015;**278**:645–659.
- McCullough CH, Ulzheimer S, Halliburton SS, et al. Coronary artery calcium: A multi-institutional, multimanager international standard for quantification at cardiac CT. *Radiology* 2007;**243**:527–538.
- Agatston AS, Janowitz WR, Hildner FJ, et al. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* 1990;**15**:827–832.
- Touboul PJ, Hennerici MG, Meairs S, et al. Mannheim carotid intima-media thickness and plaque consensus (2004–2006–2011). An update on behalf of the advisory board of the 3rd, 4th and 5th watching the risk symposia, at the 13th, 15th and 20th European Stroke Conferences, Mannheim, Germany, 2004, Brussels, Belgium, 2006, and Hamburg, Germany, 2011. *Cerebrovasc Dis* 2012;**34**:290–296.
- Gudmundsson EF, Gudnason V, Sigurdsson S, et al. Coronary artery calcium distributions in older persons in the AGES-Reykjavik study. *Eur J Epidemiol* 2012;**27**:673–687.
- Björk J, Strömberg U, Rosengren A, et al. Predicting participation in the population-based Swedish cardiopulmonary bio-image study (SCAPIS) using register data. *Scand J Public Health* 2017;**45**:S45–S49.
- Djekic D, Angerås O, Lappas G, et al. Impact of socioeconomic status on coronary artery calcification. *Eur J Prev Cardiol* 2018;**25**:1756–1764.
- Tinana A, Mintz GS, Weissman NJ. Volumetric intravascular ultrasound quantification of the amount of atherosclerosis and calcium in nonstenotic arterial segments. *Am J Cardiol* 2002;**89**:757–760.
- Tota-Maharaj R, Al-Mallah MH, Nasir K, et al. Improving the relationship between coronary artery calcium score and coronary plaque burden: Addition of regional measures of coronary artery calcium distribution. *Atherosclerosis* 2015;**238**:126–131.
- Burke AP, Kolodgie FD, Farb A, et al. Morphological predictors of arterial remodeling in coronary atherosclerosis. *Circulation* 2002;**105**:297–303.
- McClelland RL, Chung H, Detrano R, et al. Distribution of coronary artery calcium by race, gender, and age: Results from the Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation* 2006;**113**:30–37.
- Pletcher MJ, Tice JA, Pignone M, et al. What does my patient's coronary artery calcium score mean? Combining information from the coronary artery calcium score with information from conventional risk factors to estimate coronary heart disease risk. *BMC Med* 2004;**2**:31–31.
- Okwuosa TM, Greenland P, Ning H, et al. Distribution of coronary artery calcium scores by Framingham 10-year risk strata in the MESA (Multi-Ethnic Study of Atherosclerosis) potential implications for coronary risk assessment. *J Am Coll Cardiol* 2011;**57**:1838–1845.
- Pletcher MJ, Sibley CT, Pignone M, et al. Interpretation of the coronary artery calcium score in combination with conventional cardiovascular risk factors: The Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation* 2013;**128**:1076–1084.
- Fernández-Friera L, Peñalvo JL, Fernández-Ortiz A, et al. Prevalence, vascular distribution, and multiterritorial extent of subclinical atherosclerosis in a middle-aged cohort: The PESA (Progression of Early Subclinical Atherosclerosis) Study. *Circulation* 2015 Jun 16; **131**:2104–2113.
- Romanens M, Sudano I, Adams A, et al. Advanced carotid atherosclerosis in middle-aged subjects: Comparison with PROCAM and SCORE risk categories, the potential for reclassification and cost-efficiency of carotid ultrasound in the setting of primary care. *Swiss Med Wkly* 2019;**149**:w20006.
- Romanens M, Bødtker Mortensen M, Sudano I, et al. Extensive carotid atherosclerosis and the diagnostic accuracy of coronary risk calculators. *Prev Med Rep* 2017; **6**:182–186.
- National Institute for Health and Care Excellence. *Lipid modification: Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease*, London: National Institute for Health and Care Excellence, 2014.
- Näslund U, Ng N, Lundgren A, et al. Visualization of asymptomatic atherosclerotic disease for optimum cardiovascular prevention (VIPVIZA): A pragmatic, open-label, randomised controlled trial. *Lancet* 2019;**393**:133–142.