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Abstract

Aims: Coronary artery calcification (CAC) measured on cardiac CT is an important risk marker for cardiovascular disease (CVD) and has been included in the prevention guidelines. The aim of this study was to describe CAC score reference values in the middle-aged and elderly population and to develop a freely available CAC calculator.

Methods: All participants from two population-based cardiac CT screening cohorts (DanRisk and DANCAVAS) were included. The CAC score was measured as a part of a screening session. Positive CAC scores were log-transformed and nonparametrically regressed on age for each gender, and percentile curves were transposed according to proportions of zero CAC scores.

Results: Men had higher CAC scores than women, and the prevalence and extend of CAC increased steadily with age. An online CAC calculator was developed, http://flscripts.dk/cacscore. After entering sex, age and CAC score, the CAC score percentile and the coronary age are depicted including a figure with the specific CAC score and 25%, 50%, 75% and 90% percentiles. The specific CAC score can be compared to the entire background population or only those without prior CVD.

Conclusion: This study provides modern population-based reference values of CAC scores in men and woman and a freely accessible online CAC calculator. Physicians and patients are very familiar with blood pressure and lipids, but unfamiliar with CAC scores. Using the calculator makes it easy to see if a CAC value is low, moderate or high, when a physician in the future communicate and discusses a CAC score with a patient.

Key words: coronary artery disease, CAC score, CT imaging, epidemiology, percentile curve

1. Introduction

According to the European Heart Network, cardiovascular disease (CVD) causes 3.9 million deaths annually in Europe and accounts for 45% of all deaths in Europe. Ischaemic heart disease alone causes 19% and 20% of all death among men and women, respectively.[1] Ischaemic heart disease is often silent until acute myocardial infarction (MI) is evident, but subclinical coronary artery disease is easily detected by non-contrast cardiac-CT (NCCT) as calcifications located in the coronary arteries. The Agatston method is used to quantify the coronary artery calcifications (CAC) which are commonly expressed as CAC scores.[2] CAC is increasing with age, and men have higher CAC scores than women.[3,4] In a population, in which CAC is absent, there is a low risk of future CVD,[5] but as the CAC score increases, so does the risk of ischaemic heart disease.[6,7] Thus, to prevent CVD, a CAC screening to identify and target high risk individuals might be of relevance.

The importance of CAC score measurements has been studied in research over decades, and CAC score measurements have recently been included in the European and American guidelines (Class IIb, Level B and Class IIa, Level B, respectively).[8,9] Still, systematic CAC screening has not been implemented in clinical practice. One reason might be the lack of randomized clinical trials evaluating how to use the CAC score in CVD prevention. We have recently completed recruitment for the randomized Danish Cardiovascular Screening Trial (DANCAVAS).[10] The purpose of the trial was, among others, to identify persons with a CAC score above the expected median for age and gender and to offer these persons preventive medications. The MESA study has previously published CAC score reference values by age, gender and race.[11] However, MESA was not truly population-based and the CAC scan was performed with the obsolete electron-beam or 4-detectors CT scanners. Additionally, the scans were obtained in 2000 to 2002 and, as the incidence of CVD has decreased during the last decades, the CAC score reference values may have changed.[12] The DANCAVAS trial recruited participants in Denmark from 2014 to 2019, and we used CT scanners with 64 or more detectors. In a pilot study, we observed that the median CAC scores were higher than the median CAC scores published in the MESA study;[13] additionally, the differences were amplified with increasing age. We therefore had to establish our own CAC score reference values.

The primary aim of this study is to compute population-based CAC score percentiles in Danish women and men aged 50 to 75 years and make these freely available through an online calculator. The analyses are based on the DANCAVAS trial and a preceding study, called DanRisk.[14]

2. Methods

2.1 Study participants

2.1.1 The Danish Risk Score study (DanRisk)

DanRisk was a population-based survey in middle-aged men and women born in either 1949 or 1959 and living in the Southern region of Denmark. In total, 1,257 subjects (69%) from a random sample of 1,825 subjects accepted the baseline NCCT examination in 2009/2010,[14] and 1,006 participated in the follow-up examination in 2014/2015.[15] There were no exclusion criteria. The objective of DanRisk was twofold: to examine the prevalence of CAC in middle-aged Danes and to compare CAC score with the traditional risk factors. The participants were examined in one of the four regional centres (Odense, Esbjerg, Svendborg, and Vejle). The participants filled out a questionnaire concerning medical conditions (including self-reported CVD, hypertension, hypercholesterolemia and diabetes mellitus), current medication, smoking habits, and family history of CVD. Self-reported CVD was classified as previous stroke, atrial fibrillation (AF), MI, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), heart valve surgery, and peripheral arterial surgery. A personal interview on the day of examination complemented the medical history. Weight, height and blood pressure was measured. Hypertension was defined as diastolic blood pressure >90 mm Hg, systolic blood pressure >140 mm Hg, use of antihypertensive medications (thiazide, beta blockers, ACE, calcium antagonist), or self-reported hypertension by the participants. Additionally, blood tests were performed including total cholesterol, LDL, HDL and non-fasting blood glucose. If blood glucose was ≥6.1 mmol/L, fasting plasma blood glucose was measured on a second day to rule in or rule out diabetes.

2.1.2 The Danish Cardiovascular Screening Trial (DANCAVAS)

The DANCAVAS trial was a population-based, randomized cardiovascular screening trial that was performed from 2014 to 2019.[10] The objective of DANCAVAS is to investigate whether an advanced cardiovascular NCCT examination will prevent death and cardiovascular events and whether the possible health benefits are cost-effective. Outcomes are expected to be published in 2022. The main target group consisted of men aged 65-74 years,[16] but a sample of men aged 60-64 and women were invited in order to be able to estimate the benefit and cost-effectiveness by modeling.[13,17] All men (approximately 78,000), who were born in the period 1940-1957 and lived in the municipality of Odense, Nykøbing, Svendborg, Vejle, and Silkeborg, were identified by their Central Person Registration (CPR) number.[18] Approximately 22,000 of these were randomly invited to the examination. In addition, 1,200 women, who were born in the period 1940-1951 and lived in the municipality of Odense, were randomly invited. Approximately 15,000 men and 750 women accepted the invitation and were examined. There were no exclusion criteria. A questionnaire concerning prior medical history was sent along with the letter of invitation, and a medical interview was conducted with a review of this questionnaire. The questionnaire evaluated the following: self-reported CVD, hypertension, diabetes mellitus, current medication, history of smoking, and family history of CVD. Self-reported CVD was classified as in DanRisk, but did also include aneurysm. Weight, height, hip size, waist size, and blood pressure were measured. Hypertension was defined as diastolic blood pressure >100 mm Hg, systolic blood pressure >160 mm Hg, use of antihypertensive medications or self-reported hypertension by the participants. Additionally, blood tests were performed including total cholesterol, LDL, HDL, and $HgbA_{1c}$.

2.2 Measurement of CAC

To measure the CAC score, a NCCT scan was performed in the DanRisk study and the DANCAVAS trial.

2.2.1 DanRisk

Two centres (Odense and Svendborg) used a GE 64-slice CT-scanner (Discovery VCT; GE Healthcare). The scan was performed with the following parameters: gantry rotation time 500 ms, 16 * 2.5 mm collimation, 120 kV tube voltage, 200 mA tube current, and a prospectively EGC-triggered scan

acquisition gating at 50% of the R-R interval. The third centre (Vejle) used a Siemens 64-slice Dual Source CT-scanner (Siemens Definition; Siemens Medical Solutions) with the following parameters: gantry rotation time 330 ms, 3.0 mm collimation, 100-120 kV tube voltage, 150 mA tube current, and prospective gating at 60% of the R-R interval. The fourth centre (Esbjerg) used a Toshiba 64-slice CT-scanner (Aquilion; Toshiba Medical Systems) with the following technical settings: gantry rotation time 450 msec, 3 mm collimation, 120 kV tube voltage, and prospective gating at 75% of the R-R interval. In all cases the scan data were acquired during an inspiratory breath hold. The Agatston score was calculated by summing-up the scores from each of the foci found in the coronary arteries.

2.2.2 DANCAVAS

In two centres (Odense and Vejle), the NCCT was performed using a Siemens Somatom Definition Flash 128 slice Dual Source or a Somatom Force scanner (Flash: gantry rotation time 0.28 s, 3.0 mm collimation, acquisition 128x0.6 mm, 120 kV tube voltage, 90 mAs tube current. Force: gantry rotation time 0.25 s, 3.0 mm collimation, acquisition 38x1.2 mm, 120 kV tube voltage, 80 mAs tube current). Imaging was prospectively ECG-triggered at 70% of the R-R interval if the heart rate was <75 or at 250 to 300 ms after the QRS-complex if the heart rate was >75. A third centre (Nykøbing) used a Philips iCT 256 slice scanner (gantry rotation time 0.27 s, 2.5 mm collimation, auto acquisition 128x0.625, 112x0.625 or 96x0.625 mm, 120 kV tube voltage, 50 mAs tube current). Imaging was prospectively ECG-triggered at 75% of the R-R interval at all heart rates. A fourth centre (Silkeborg) used a Toshiba Aquilion One 320 slice scanner (gantry rotation time 0.35 s, acquisition collimation 320x0.5 mm, 120 kV tube voltage, 28 mAs tube current). Imaging was prospectively ECG-triggered at 75%, exposure window 450 ms, of the R-R interval if the heart rate was <65 or at 40%, exposure window 450 ms if the heart rate was >65. The fifth centre (Svendborg) used a GE Healthcare Revolution scanner (gantry rotation time 0.28 s, 2.5 mm collimation, smart coverage acquisition 256x0.625, 224x0.625 or 192x0.625 mm, 120 kV tube voltage, 15 mAs tube current). Imaging was prospectively ECG-triggered at 75% of the R-R interval if the heart rate was <75 or at 350 ms after the QRS-complex if the heart rate was >75.

2.3 Statistical analysis

The distribution of the CAC score follows usually a right-skewed distribution with a large proportion of participants having a CAC score of 0. The log-transformed CAC score distribution of patients with a positive CAC score (i.e. CAC score >0) follows, though, a quite symmetric and bell-shaped distribution. In obtaining the desired percentiles of the overall CAC score distribution, we followed the methodology of the MESA study.[11]

First, we modelled the mean of the log CAC score distribution nonparametrically as a function of age for each gender using a local regression smoother with a bandwidth of 0.8.[19] For each observation in the positive, log-transformed CAC score distribution, we subtracted the corresponding estimated value. The pooled residuals from this model were then ranked, and we calculated the j-th percentile for each of j=1,…,99 of the residuals. Adding these to the model-based value for a particular age and gender yielded an estimated percentile for the log-transformed, positive CAC variable.[20] Applying the exponential function to the percentiles transformed these back to the original scale for the CAC score and yielded the j-th percentile of the distribution of patients with a positive CAC score.

If a certain proportion p has a CAC score of 0, then the j-th percentile calculated above is the 100*{p+[(1-p)j]/100} percentile of the overall distribution. For instance, if the median CAC score in CAC-positive, 60-year old, male patients is 85, and the proportion p is 0.3 in that group, then this CAC score of 85 is the 100*{0.3+[(1-0.3)*50]/100}=65th percentile of the overall distribution for men aged 60. The median of the 70% of participants with a positive CAC score “moves” on top of 30% of participants with a CAC score of zero and becomes the 65th percentile of the respective overall distribution.

We modelled p as a nonparametric function of age by fitting a local regression smoother (with a bandwidth of 0.8 as before) within each gender. By this means, we estimated the percentiles of the whole distribution for a given gender and age as a function of the percentiles of the positive CAC scores, and this process did not involve any parametric assumptions.

Intergroup comparisons were done with Kruskal-Wallis test. Intra- and interrater variation analysis was performed with nonparametric Limits of Agreement (employing a weighted average of the

observations closest to the target quantile) due to high proportions of zero differences and non-normality of the distributions of differences.[21]

All analyses were performed with STATA/MP 16.1 (StataCorp, College Station, Texas 77845 USA) and are illustrated in the Supplemental Material 1.

3. Results

The aggregated dataset consisted of 2,268 scans of DanRisk and 14,984 scans of DANCAVAS participants (Table 1). The gender distribution was balanced in DanRisk, whereas 95% of DANCAVAS patients were male. The DanRisk population was, on average, 7-8 years younger than that of DANCAVAS, and family history of CVD was more pronounced in DanRisk (women: 26% vs. 18%, men: 18% vs. 14%). Hypertension was more often reported in DANCAVAS patients (women: 89% vs. 40%, men: 87% vs. 43%), as was hypercholesterolemia (women: 93% vs. 84%, men: 83% vs. 80%). Both creatinine and triglycerides levels were, on average, slightly increased in DANCAVAS patients. Stroke; MI, PCI and CABG; heart valve surgery; peripheral arterial surgery; and, hence, CVD were more often reported in DANCAVAS than in DanRisk participants. The same was true for all concomitant medication shown in Table 1, apart from oral antidiabetics and insulin in women. The median (interquartile range) CAC scores were smaller in DanRisk than in DANCAVAS participants (women: 0 (0-14) vs. 14 (0-112), men: 10 (0-117) vs. 123 (12-509)), which relates to the age differences between the study cohorts described above. The same pattern applied to the Heart Score, i.e. the Systematic Coronary Risk Estimation (SCORE). Smoking, hypertension, hypercholesterolemia, and diabetes mellitus were associated with increased CAC scores, but with considerable spread (Supplemental Material 2, Figure A). Median CAC scores (interquartile range) also increased over CV risk class (low: <3%, medium: 3-4%, high: 5-9%, very high: ≥10%), but again with huge spread within each class: 0 (0-41), 36 (0-201), 89 (8-351), 163 (28-568); p=0.0001 (Figure 1).

Around one half of women (52%) had CAC scores of zero in our sample, as opposed to 17% of men. In accordance to earlier reports,[3,11] men had higher CAC scores than women, and the prevalence and extent of CAC increased steadily with age (Figure 2). Percentile values for CAC are shown in

Supplemental Material 3, Tables I and II. Inspired by the CAC calculator based on the MESA study (https://www.mesa-nhlbi.org/Calcium/input.aspx),[11] we developed a freely accessible online calculator (http://flscripts.dk/cacscore). After entering sex, age and CAC score, the CAC score percentile and the coronary age are depicted including a figure with the specific CAC score and 25%, 50%, 75% and 90% percentiles. Two datasets are available; one with the entire population (reference values are based on 17,252 participants) and one excluding patients with prior CVD (reference values are based on 14,614 participants).

The median CAC score for women was very similar in our study, MESA (considering the subgroup of whites), and the population-based Heinz Nixdorf Recall (HNR) study (Supplemental Material 2, Figure B).[3,11] In men, the median CAC score was larger in our study than in MESA and HNR in the elderly, aged 70-75 years. Our 90th percentile for women was identical to that of the HNR study across the considered age range, but larger than that of the MESA study in those 70-75 years of age (Supplemental Material 2, Figure C).[3,11] Our 90th percentile for men was identical to that of MESA and smaller than that of HNR in the 50-65 year olds. In the upper age range (70-75 years), our 90th percentile for men exceeded that of both MESA and HNR.

Supplemental Material 2, Figures D-F, contains the sensitivity analysis for Figure 2 and Supplemental Figures B and C after exclusion of CVD patients (N=2,638). Both 50th and 90th percentile curves became flatter for women and men (Supplemental Figure D), which in turn were then identical to the MESA curves in white women and slightly below those of MESA for white men (Supplemental Figures E and F).

Intrarater variation analysis was performed as part of the DanRisk study in 129 randomly chosen participants.[14] Later, these analyses were extended by nonparametric Limits of Agreement of -62 to 13 HU and an estimated mean difference (bias) of 0 HU.[22] For interrater variation analysis, the above random sample from DanRisk was extended by 101 randomly chosen participants from the DANCAVAS study. Based on these 230 observations, the nonparametric Limits of Agreement for the interrater comparison were -83 and 38 HU, and the estimated bias was 0 HU (Supplemental Material 2, Figure G). These limits sound considerably wide; however, 12 out of 230 observations (5%) were

associated with absolute differences exceeding 50 HU most of which stemming from CAC score measurements of 400 HU or more.

4. Discussion

4.1 Statement of principal findings

In accordance with the previously published two landmark studies on CAC score reference values, the American MESA study and the German HNR study,[3,11] we found that the CAC score is increasing with age. Regarding the women, the results were very much alike, but some differences exist regarding the men. Until the age of 66, Danish men had lower CAC scores compared to German men, and from the age of 66 on Danish men had higher CAC scores compared to both German and American men.

4.2 Strengths and weaknesses of the study

The strength of this study is the population-based setup in various Danish, geographically and thus socioeconomically different areas. However, the participation rates were 69% and 62% in DanRisk and DANCAVAS, respectively, causing risk of selection bias. In the DanRisk study, we found that non-participants had a lower socioeconomic status,[23] and this is confirmed in other population-based screening trials.[24,25] As living in an area with low socioeconomic status is associated with presence of CAC,[26] this selection bias may entail that our CAC reference values are underestimated. Standardized CT protocols and use of modern cardiac-CT scans increased the external validity regarding generalisability to modern cardiac scanners. However, as the participants in this study are Danish citizens and mainly Caucasians, the results may not be applicable to other nationalities and ethnic groups. Also, the majority was men aged 60-74 years. Nonetheless, we did include almost 2,000 women.

4.3 Strengths and weaknesses of the study in relation to other studies

Based on the Danish CPR numbers, our recruitment methods secured a more transparent population-based approach compared to the MESA study. MESA recruited in six field centres in the United States, and recruitment was done using locally available sources such as motor vehicle lists, consumer lists,

voter registration lists, and lists of residents, dwellings or telephone exchanges.[11] In the HNR study,[3] recruitment was performed in an unstratified and random way through citizen registries in the German Ruhr area. Although comparable recruitment methods were applied, our participation rates were somewhat higher than the 56% reported in the HNR study, whereas the participation rate was not stated in the MESA study. While our cohort represents a true random population-based sample with a relatively high response rate, the external validity of HNR and, especially, the MESA study might suffer from a low response rate, not accurately reflecting the general populations from which they were drawn.

The MESA study included 6,814 men and women aged 45–84 years from which reference values were derived for 4 ethnicities (white, Chinese, black, and Hispanic), while the HNR study included 4,814 men and women aged 45–74 years. Thus, both studies included more women than we did, but the CAC score reference values for women seem to be alike anyway. We included far more men, and according to Supplemental Material 2, Figures B and C, Danish men aged 50-65 years apparently have lower CAC scores than German men and similar CAC scores to white American men, while elderly Danish men have higher CAC scores compared to American and German men. This is probably due to different exclusion criteria in the studies. In MESA, they excluded individuals with prior CVD, while HNR excluded individuals with a history of ischemic heart disease. We aimed to establish CAC score reference values for the background population, and, accordingly, we had no exclusion criteria. This entails increased CAC score reference values among the elderly men in our study. Nonetheless, if we excluded participants with prior CVD, the CAC scores in our study seem to be lower compared to American and German men. Furthermore, the MESA and NHR studies took place from 2000 to 2003, and the derived CAC reference values rely on analyses from the outdated electron-beam or 4-detectors CT scanners, whereas we have used contemporary cardiac CT-scanners. According to a phantom study, CAC scores obtained with 64-slice CT scanners are highly correlated with electron-beam CT scanners obtained CAC scores, but significantly underestimated.[27] Consequently, our CAC reference values would have been larger if electron-beam CT scanners had been use. Thus, our findings are in accordance with the findings from the older MESA and HNR studies.

Recently, a pooled analysis including more than 155,000 individuals has been published.[28] However, the data was not based on subjects from the general population, but comprised self-referred or physician-referred individuals. Also, the vast majority of the data were obtained from American studies and the CAC scores were obtained with the outdated EBCT scans. Their calculator had age- and sex-based percentiles up to 24 percentile points higher than the renowned MESA calculator. Unfortunately, the pooled analyses did not include the internationally acclaimed MESA and HNR studies, neither the two Danish studies reported here. We therefore believe that our calculator including data from the general population is more reliable and useful in the daily clinical work.

4.4 Meaning of the study: implications for clinicians

This study provides modern population-based reference values of CAC scores in men and woman aged 50-74 using up-to-date cardiac CT scanners. Based upon these observations, an online calculator (http://flscripts.dk/cacscore) has been made freely accessible. After entering sex, age and CAC score, the CAC score percentile and the coronary age are depicted including a figure with the specific CAC score and 25%, 50%, 75% and 90% percentiles. The specific CAC score can be compared to the entire background population or only those without prior CVD. Physicians and patients are very familiar with blood pressure and lipids, but unfamiliar with CAC scores. Using this online CAC calculator makes it quite easy to see if a value is low, moderate or high.

4.5 Unanswered questions, ongoing and future research

The current prevention guideline recommends systematic cardiovascular risk assessment, e.g. SCORE, to be used in apparently healthy people.[8,29] Low- to moderate-risk persons (SCORE <5%) should be offered lifestyle advice to maintain risk status, while high-risk persons (SCORE 5-9%) qualify for intensive lifestyle advice and may be candidates for drug treatment. Our study confirms that high CAC scores are uncommon among low-risk people, but even among persons with moderate-risk a substantial part have high CAC scores. Additionally, among persons with high-risk, a substantial part has low CAC scores. These findings are in accordance with the huge Swedish SCAPIS study.[30] Thus, our current risk stratification strategies are far from optimal leading to both under- and over-treatment of patients. Numerous studies have shown that CAC scoring improves cardiovascular risk stratification,[31]

but, unfortunately, we do not have a well-established threshold for preventive treatment. Should we prescribe preventive treatment with statin and / or aspirin to (a) all with presence of CAC, (b) those with a CAC score above a specified percentile (e.g. CAC score above 50% percentile), or (c) those with a value above a specific benchmark value (e.g. CAC score above 400)?

One randomized trial included 1,005 asymptomatic men and women age 50 to 70 years with CAC scores at or above the 80th percentile for age and gender.[32] The study participants were randomized to atorvastatin 20 mg versus placebo, and all received aspirin 81 mg daily. The treatment failed to significantly reduce CVD events, but may have reduced the event rate in participants with baseline CAC score above 400. In the very huge ROBINSCA trial, asymptomatic men aged 45-74 years and women aged 55-74 years were randomized to a CT-based screening trial for CAC scoring.[33] Patients with CAC score > 100 were referred to their general practitioners for further cardiovascular risk management. Study inclusion has completed, but end-points are so far not published.[34] In our own DANCAVAS trial, we have randomized men aged 65-74 years to usual care or an advanced cardiovascular screening examination including NCCT, ankle and brachial blood pressure measurements, and blood tests. Regarding the CAC score, we initiated statin and aspirin treatment, if the CAC score was above the expected median. Results are expected to be published in 2022.

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Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Authors' Contributions

OG and ACPD conceived and designed the study. JSL, JL, LF, FHS, MK, KE, GU, MB and HM played key roles in recruitment of participants and contributed to the acquisition, analysis, or interpretation of data for the work. OG and ACPD drafted the report, with key input from BHA. All authors provided critical input into revised versions of the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Figure legends

Figure 1. Boxplots for CAC score by CV risk class (low: <3%, medium: 3-4%, high: 5-9%, very high: ≥10%) after exclusion of CVD patients.

Figure 2. Percentile curves (25^{th}, 50^{th}, 75^{th}, and 90^{th}) over age by gender.

Appendices

None

Supplemental Material

Supplemental Material 1: Details and visualizations of intermediate steps in deriving percentile curves.

Supplemental Material 2: Supplemental Figures A-G.

Supplemental Material 3: Supplemental Tables I and II.

Table 1. Demographics and clinical baseline characteristics of the study population

Variable	DanRisk (N=2,268)		DANCAVAS (N=14,984)	
	Women	Men	Women	Men
Number of scans	1,185 (52%)	1,083 (48%)	745 (5%)	14,239 (95%)
Number of participants	643 (53%)	578 (47%)	745 (5%)	14,239 (95%)
Age, years	60 (49-66)	60 (49-67)	68 (63-75)	67 (60-75)
Smoking:				
• Non-smokers	613 (52%)	457 (42%)	384 (52%)	4,688 (33%)
• Former smoker	339 (29%)	349 (32%)	261 (35%)	7,201 (51%)
• Active smokers	233 (20%)	277 (26%)	98 (13%)	2,291 (16%)
• Unknown	0 (0%)	0 (0%)	2 (0.3%)	59 (0.4%)
Family history of CVD	308 (26%)	196 (18%)	135 (18%)	2,007 (14%)
BMI, kg/m^2	26.8 (5.2)	27.6 (4.3)	26.7 (5.0)	28.1 (4.4)
Waist size, cm	90 (13)	99 (11)	90 (13)	103 (12)
Systolic blood pressure, mmHg	134 (20)	138 (17)	155 (20)	149 (19)
Diastolic blood pressure, mmHg	80 (11)	83 (10)	83 (9)	82 (10)
Hypertension	479 (40%)	467 (43%)	666 (89%)	12,358 (87%)
HDL, mmol/L	1.7 (0.5)	1.4 (0.4)	1.7 (0.5)	1.4 (0.4)
LDL, mmol/L	3.2 (0.9)	3.2 (0.9)	3.2 (1.0)	2.9 (1.0)
Total cholesterol, mmol/L	5.5 (1.0)	5.3 (1.0)	5.6 (1.1)	5.0 (1.1)
Hypercholesterolemia	993 (84%)	861 (80%)	694 (93%)	11,753 (83%)
Creatinine (µmol/L)	66 (12)	82 (21)	74 (29)	89 (23)
Triglycerides, mmol/L	1.2 (0.4-9.3)	1.5 (0.3-10.0)	1.5 (0.5-7.8)	1.6 (0.3-16.5)
Diabetes	69 (6%)	68 (6%)	59 (8%)	1,796 (13%)
CVD	26 (2%)	56 (5%)	88 (12%)	2,451 (17%)
• Stroke	19 (2%)	20 (2%)	59 (8%)	898 (6%)
• MI, PCI, CABG	5 (0.4%)	29 (3%)	20 (3%)	1,367 (10%)
• heart valve surgery	1 (0.1%)	5 (0.5%)	4 (0.5%)	155 (1%)
• peripheral arterial surgery	1 (0.1%)	5 (0.5%)	14 (2%)	319 (2%)
Statins	201 (17%)	185 (17%)	271 (36%)	4,688 (33%)
Thiazide	145 (12%)	93 (9%)	149 (20%)	1,660 (12%)
Beta blockers	88 (7%)	72 (7%)	108 (15%)	2,161 (15%)
ACE inhibitors or ARBs	189 (16%)	189 (18%)	222 (30%)	4,734 (33%)
Calcium antagonists	83 (7%)	94 (9%)	110 (15%)	2,730 (19%)
Oral anti-diabetic	41 (4%)	37 (3%)	31 (4%)	1,150 (8%)
Insulin	41 (4%)	37 (3%)	31 (4%)	1,150 (8%)
SCORE[a]	1 (0.5-2.1)	2.7 (1.5-4.5)	5 (3.3-7.8)	6.9 (4.8-10.1)
CAC score	0 (0-14)	10 (0-117)	14 (0-112)	123 (12-509)

Numbers are n (%), mean (SD) and median (interquartile range). ACE, Angiotensin-converting enzyme; ARBs, Angiotensin II receptor blockers; BMI, body mass index; CABG, coronary artery bypass graft; CAC, coronary artery calcium; CVD, cardiovascular diseases; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; MI, myocardial infarction; PCI, percutaneous coronary intervention; SCORE, Systematic Coronary Risk Estimation. [a]Based on patients without prior CVD (N=14,614).

Figure 1

Click here to access/download;Figure;Fig1_cv_risk.tif

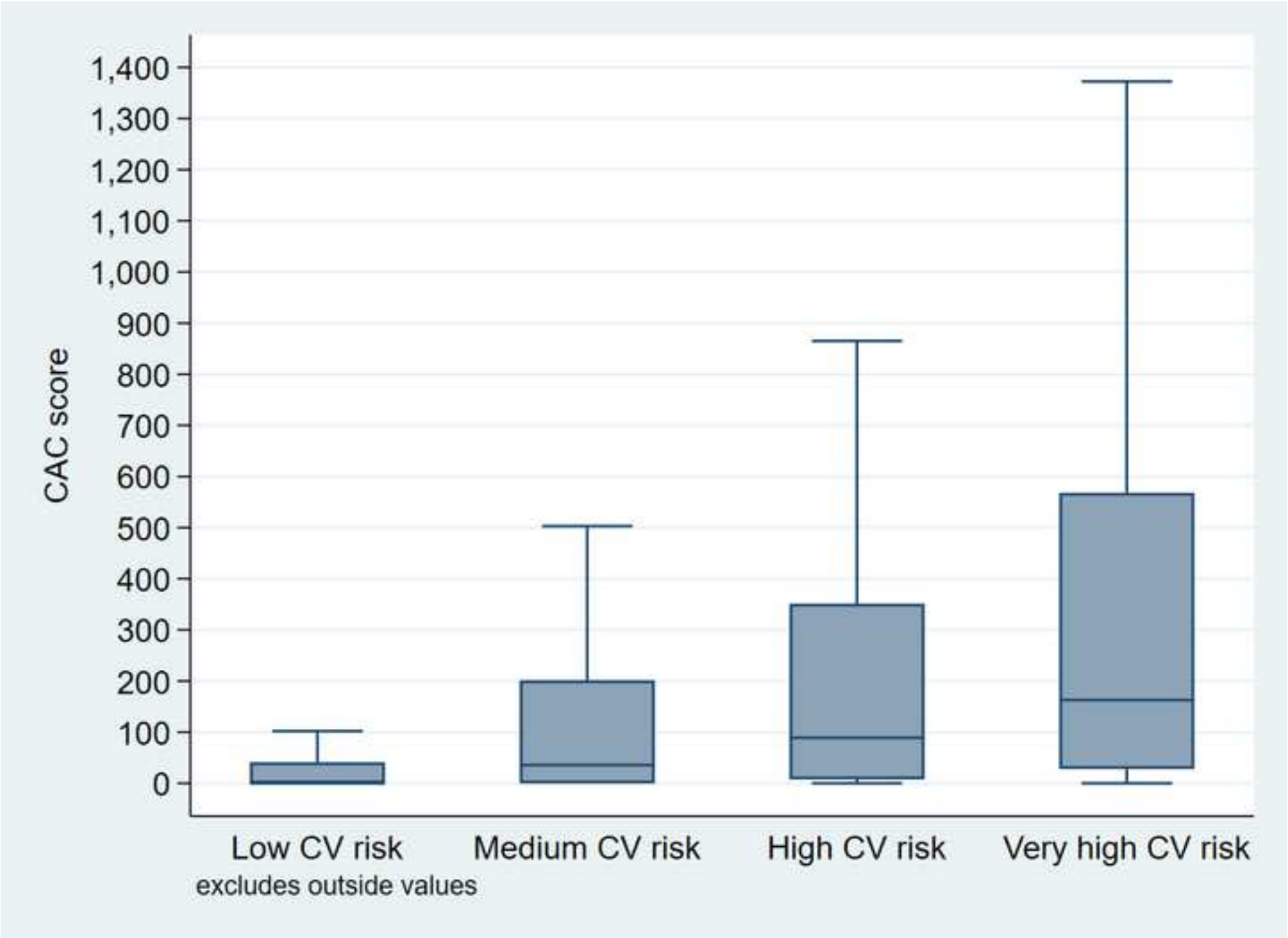
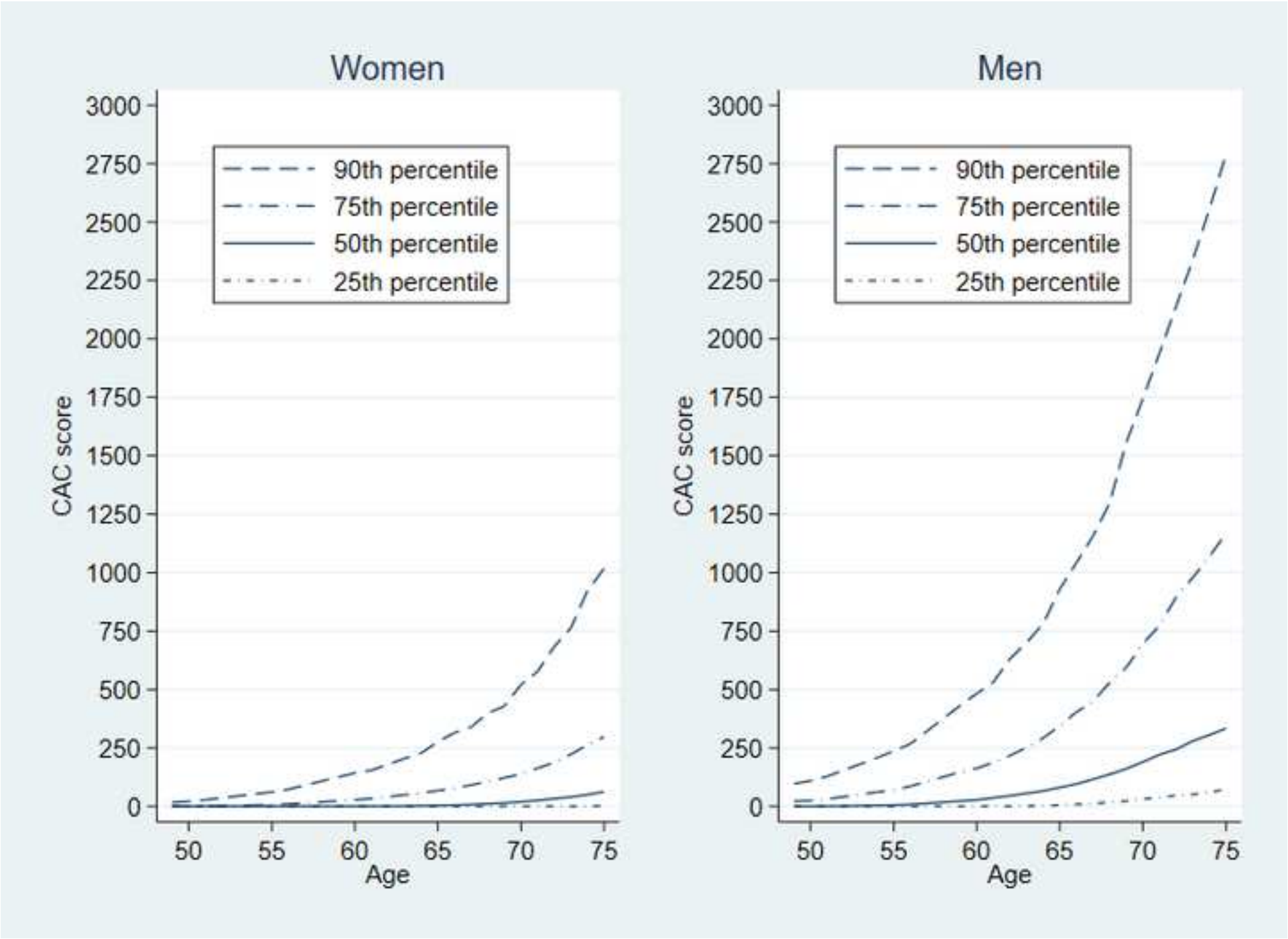


Figure 2



Supplemental Figures

Supplemental Tables