SUPPLEMENTAL MATERIAL

Supplement to: Bergström G, Persson M, Adiels M, et al. Prevalence of subclinical coronary artery atherosclerosis in the general population

Contents

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The Swedish CArdioPulmonary bioImage Study (SCAPIS) is a collaborative project between the following Swedish Universities and Swedish University Hospitals:
University of Gothenburg and Sahlgrenska University Hospital; Karolinska Institutet and Karolinska University Hospital; Linköping University and Linköping University Hospital; Lund University and Skåne University Hospital; Umeå University and University Hospital of Umeå; Uppsala University and Uppsala University Hospital.

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METHODS

Reproducibility and consistency of reading CCTA across readers and sites

Reproducibility of reading CCTA images was tested between two readers who repeated their assessment of 51 consecutive cases >4 weeks apart (**Table V** in the Supplement). In these readings, 10 of the 11 most proximal segments, but not segment 9 (first diagonal), were included.

To check for consistency of data across readers and sites, the relation between CCTA data and coronary artery calcium score (CACS) was examined given that CACS is considered to be less user-dependent than CCTA and there is a positive association between CACS and the extent of coronary atherosclerosis.[41,49] Frequency of the CCTA outcome (no atherosclerosis, 1-49% stenosis, ≥50% stenosis or calcium blooming) was plotted in relation to CACS categories for individual readers (**Figure II** in the Supplement) and for each site (**Figure III** in the Supplement).

Definitions of CCTA scores used to calculate burden of coronary atherosclerosis per subject

In the current paper, the following anatomical assumptions were made to define the three main coronary vessels:

Left anterior descending artery (LAD): (S5, S6, S7, S8, S9, S10 and S17)

Left circumflex artery (CXA): (S11, S12, S13, S14, S15, S18)

Right coronary artery (RCA): (S1, S2, S3, S4, S16)

One-vessel, two-vessel or three-vessel disease was then defined by a ≥50% stenosis in one, two or three of the above vessels.

Inverse probability for participation weighting (IPPW)

To test external validity, prevalence measures of coronary atherosclerosis were standardized the age-matched population in the SCAPIS catchment areas, which reflects the population that was invited to participate in SCAPIS or Sweden as a whole using sociodemographic register data and inverse probability for participation weighting (IPPW).[50, 51]

With assistance from Statistics Sweden, the SCAPIS participants were matched to each of the 5,985 demographic statistics areas (DSAs) in Sweden (1,925 of which are located within the SCAPIS catchment areas) using home addresses. DSAs are nested within municipalities and defined with respect to geography and population size, and their primary purpose is to monitor social segregation at a fine scale. The average population size of a DSA is ~300 (range: 0-719) for the population aged 50-64 years.

For each DSA, we asked Statistics Sweden to supply yearly data from 2013 to 2018 on the following covariates: (i) the median income per household, (ii) the percentage of immigrants born in non-western countries (Africa, Asia, Eastern Europe and South America), (iii) the proportion of individuals aged 50-64 with tertiary education, (iv) the unemployment rate for the population 20-64 years and, (v) population size by age group and sex. If a DSA was within the catchment areas for SCAPIS, we averaged these variables over the enrollment period for each site; for all other DSAs outside the SCAPIS catchment areas, we used mean values across the period 2013-2018. We used the data to characterize the SCAPIS participant dataset and two target populations of interest to SCAPIS: (1) the age-matched population in the SCAPIS catchment areas, which reflects the population that was invited to participate in SCAPIS, and (2) the entire Swedish population (aged 50-64 years).

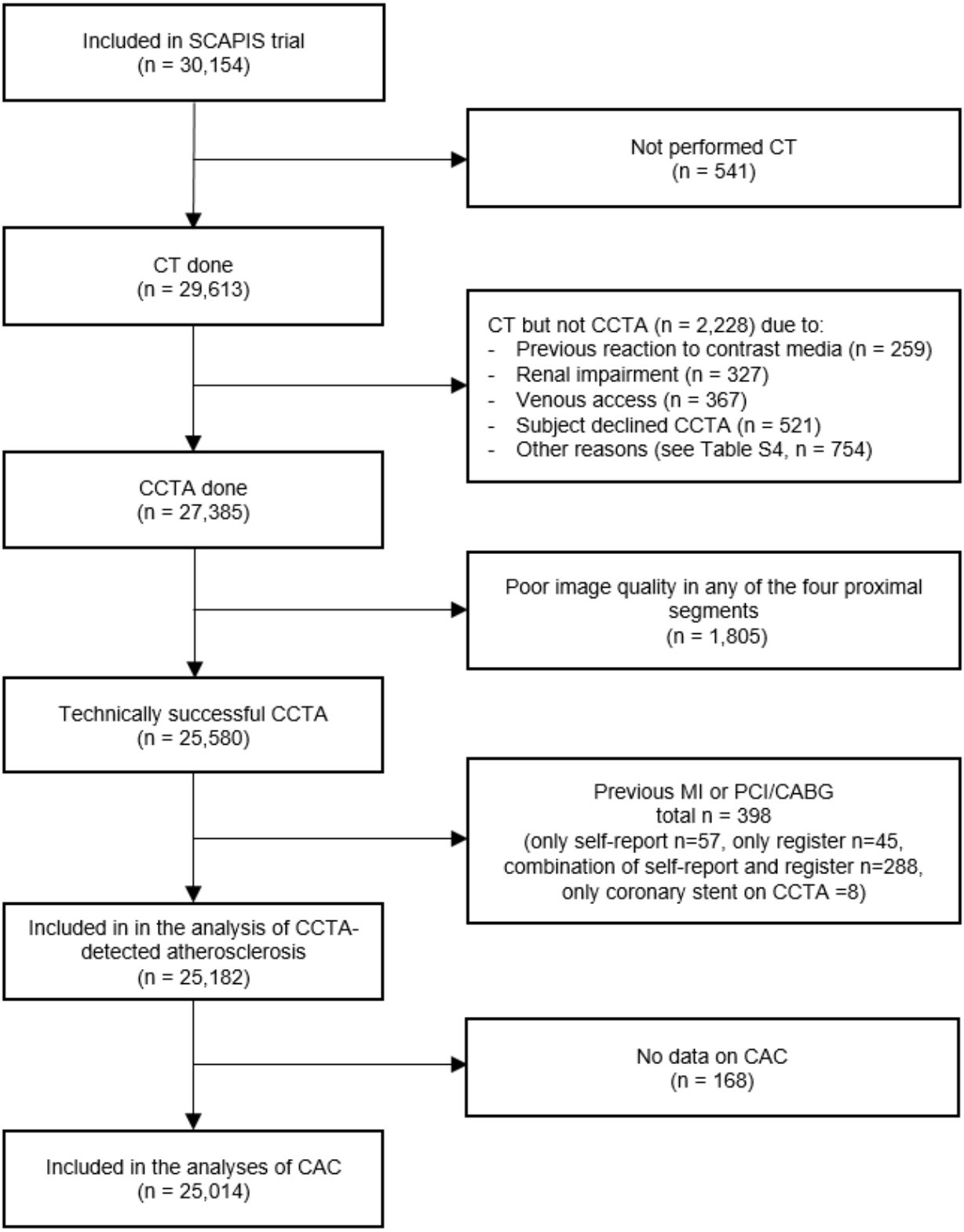
We estimated two sets of inverse-odds-of-participation weights to standardize the SCAPIS sample to match each of these target populations on the distribution of DSA-level sociodemographic characteristics, as well as age group and sex. We stacked the two focal target populations data on top of the SCAPIS dataset and coded a participation dummy as “one” for participants and “zero” for the population.[51] We then used logistic generalized additive models with cubic splines to model the odds of belonging to the SCAPIS sample.[51]

Independent variables included in the models were age group, sex and the DSA-level characteristics. The inverse of the predicted odds of these models was then used to obtain the weighted estimates presented in **Table VII** in the Supplement.

Handling of calcium blooming

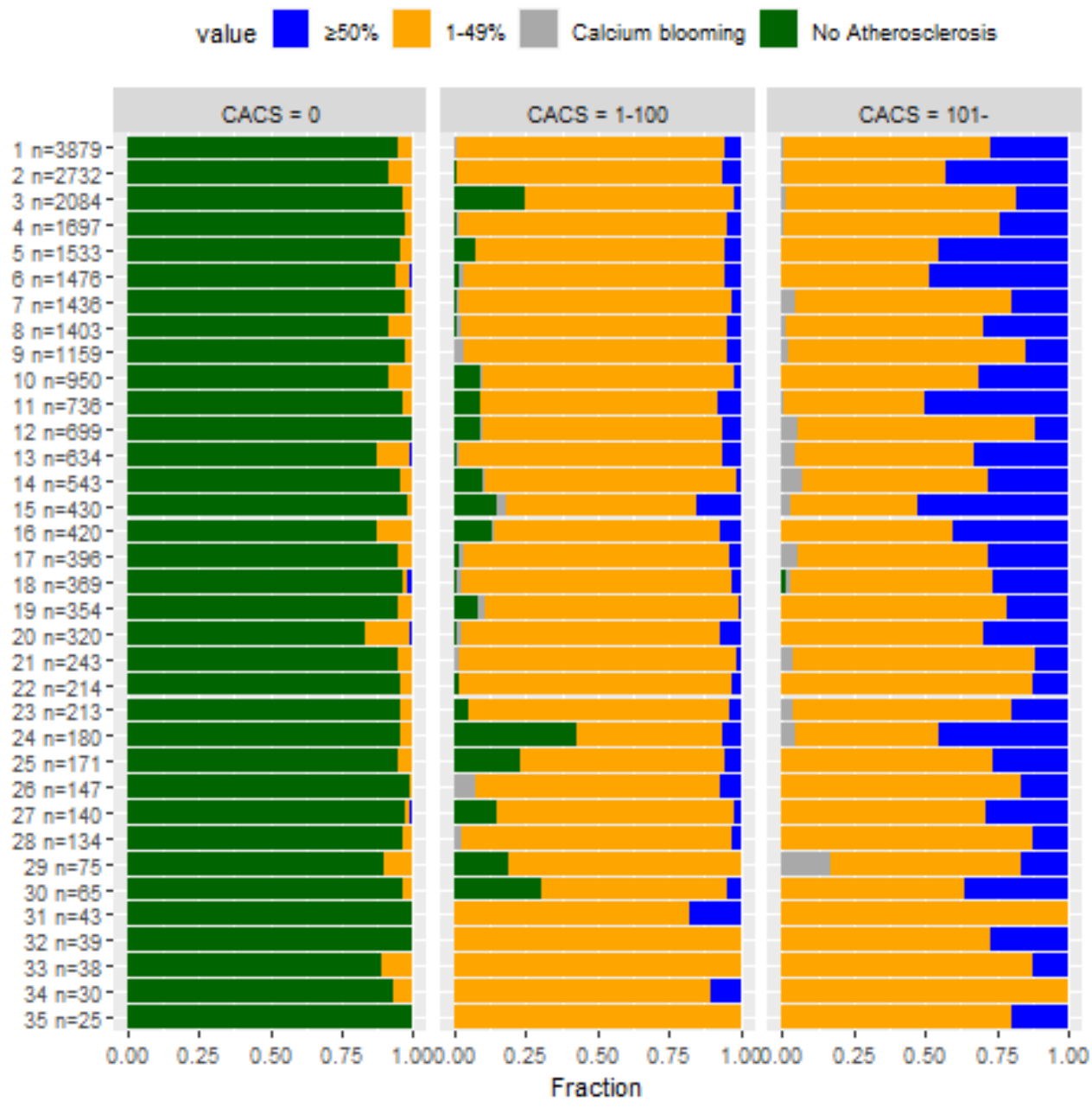
Defining the level of stenosis from calcified plaques is a challenge for CCTA and calcifications are known to overestimate the level of stenosis;[21,22] indeed, one study reported that only 29% of severely calcified segments were associated with significant obstructive disease.[21] If calcium content of the segment was severe and precluded judgement of level of stenosis, the segment was classified as having a calcium blooming artefact and, in the main analyses, the level of stenosis was set to 1-49%. In a sensitivity analysis presented in **Table IX** in the Supplement, the level of stenosis for a calcium blooming artefact was set to ≥50%.

SUPPLEMENTARY FIGURES



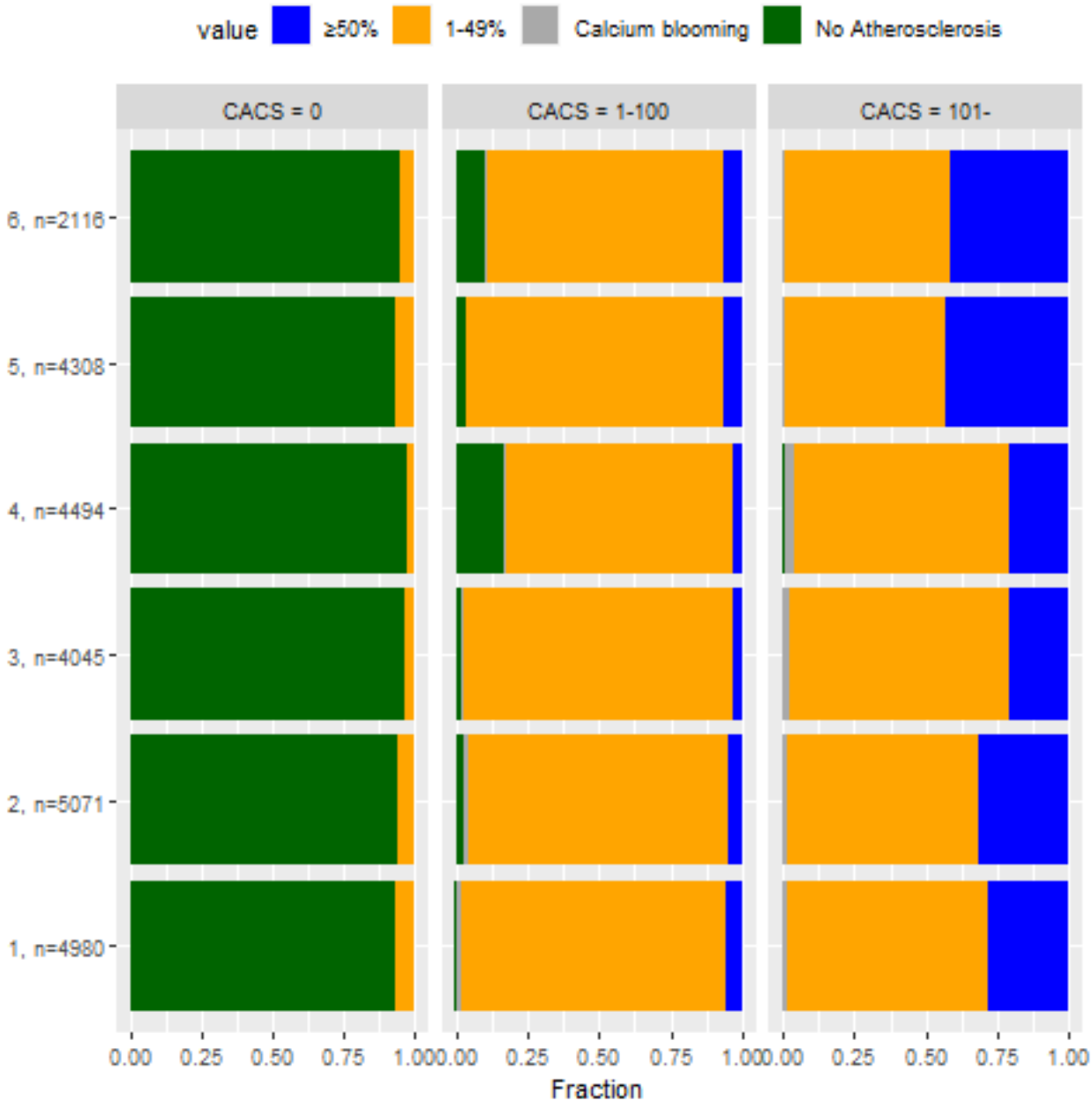
Supplemental Figure I: Flow diagram of study inclusion.

MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.



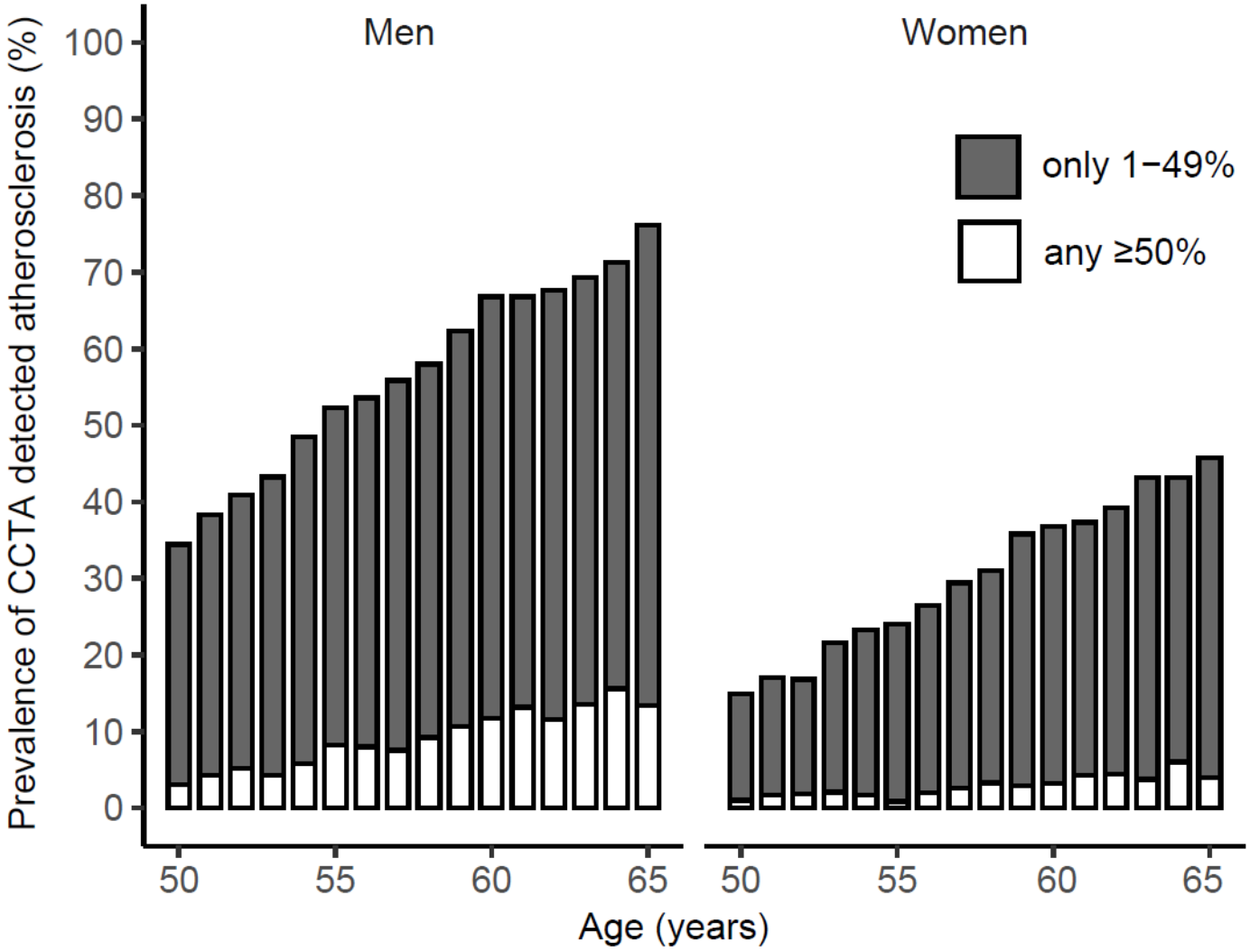
Supplemental Figure II: Atherosclerosis per subject for individual readers, stratified by CACS category.

Each subject was classified according to the highest segmental burden of coronary atherosclerosis (in increasing order: no atherosclerosis; calcium blooming; 1-49% stenosis; or ≥50% stenosis) in the 11 most proximal segments. Data reported from the 35 readers with at least 10 cases read (there were 37 readers in total) and n= 25,014 cases (CAC data were missing in 168 subjects).



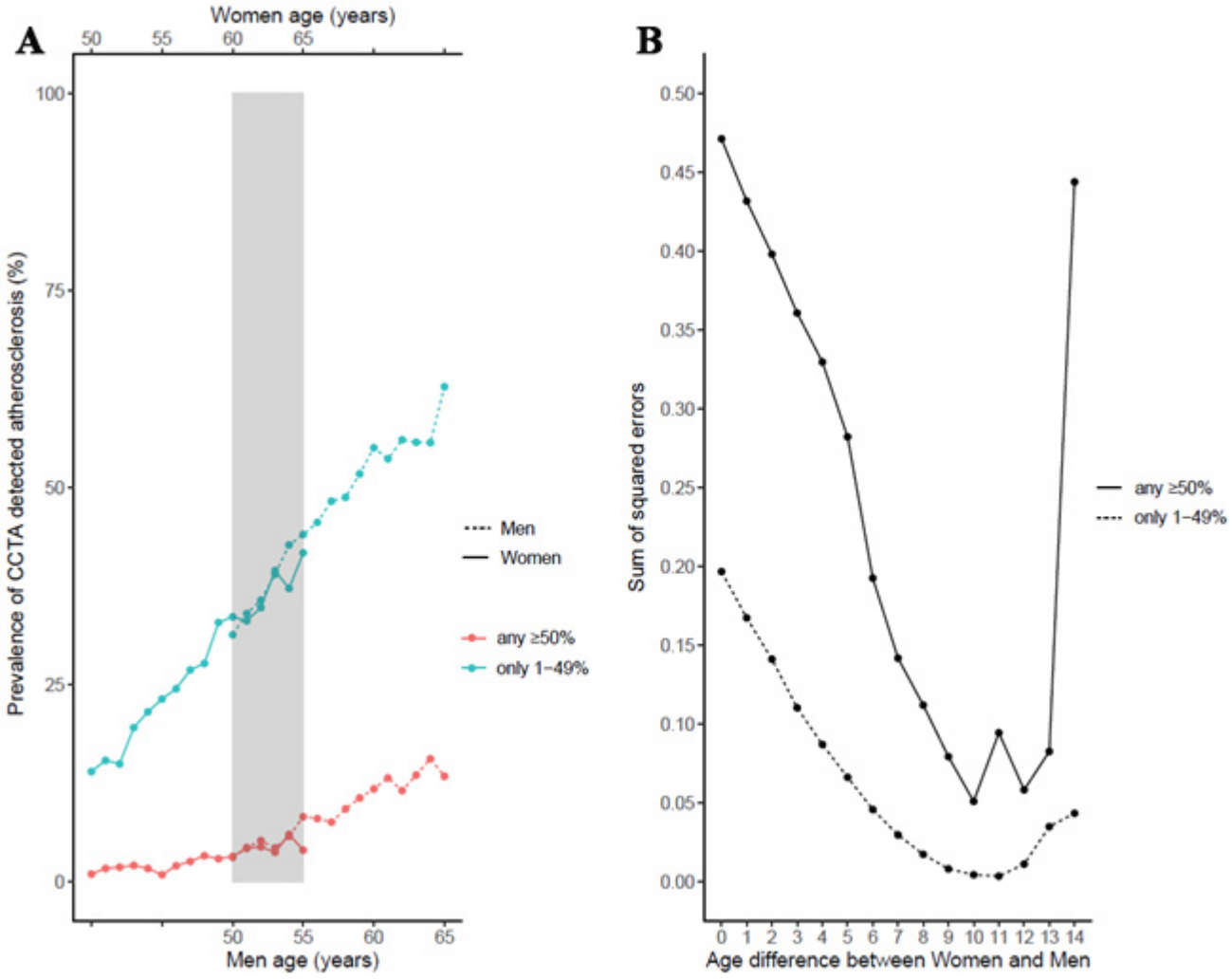
Supplemental Figure III: Atherosclerosis per subject for each site, stratified by CACS category.

Each subject was classified according to the highest segmental burden of coronary atherosclerosis (in increasing order: no atherosclerosis; calcium blooming; 1-49% stenosis; or ≥50% stenosis) in the 11 most proximal segments. Data reported per site and n= 25,014 (CACS data were missing in 168 subjects).



Supplemental Figure IV: Prevalence of CCTA-detected atherosclerosis by sex and age.

Prevalence of CCTA-detected coronary atherosclerosis and degree of stenosis in the SCAPIS cohort (n=25,182), divided by sex and age.



Supplemental Figure V: Modeling of delayed onset of coronary atherosclerosis in women.

The delayed onset of CCTA-detected atherosclerosis (any ≥50% stenosis and only 1-49% stenosis) in women compared to men was modeled by sliding the x-axis for women back and forth in relation to that of men (Panel A) in 1-year intervals, and identifying the minimal value of the sum of the squared differences between the annualized prevalence in women and men (Panel B).

SUPPLEMENTARY TABLES

Supplemental Table I. Characteristics of study participants in the full SCAPIS cohort.

Characteristic	Total	Men	Women
Sample size — n	30,154	14,646	15,508
Sociodemographics			
Age — years	57.5±4.4	57.5±4.4	57.5±4.3
Education, university degree — n (%)	13,218 (45.1)	5,769 (40.7)	7,449 (49.2)
Employed — n (%)	24,483 (81.2)	11,992 (81.9)	12,491 (80.5)
Anthropometry			
Body mass index at age 20 — kg/m^2	21.9±2.7	22.8±2.5	21.1±2.7
Body mass index — kg/m^2	27±4.5	27.5±4	26.5±4.9
Waist circumference — cm	94.4±13	99.8±11.2	89.4±12.5
Behavior			
Smoking status			
Current smoker — n (%)	3,728 (12.7)	1,798 (12.6)	1,930 (12.7)
Former smoker — n (%)	10,602 (36.0)	4,761 (33.4)	5,841 (38.5)
Mean pack years	7.5±12	7.5±12.6	7.4±11.3
Duration of smoking — years	11.8±15.6	11.2±15.5	12.5±15.7
Alcohol use			
Once per month or less — n (%)	7,198 (24.7)	2,909 (20.6)	4,289 (28.5)
2-4 times per month — n (%)	11,123 (38.1)	5,391 (38.2)	5,732 (38.0)
More than once a week — n (%)	10,865 (37.2)	5,816 (41.2)	5,049 (33.5)
Physical activity			
Time spent sedentary — % of active time	54±10.5	55.9±10.5	52.2±10.1
Time in moderate or vigorous activity — % of active time	6.4±3.4	6.6±3.6	6.2±3.2
Treatment			
Cholesterol-lowering medication — (%)	2,297 (7.6)	1,386 (9.5)	911 (5.9)
Antihypertensive medication — n (%)	5,768 (19.1)	3,034 (20.7)	2,734 (17.6)
Diabetes medication — n (%)	1,074 (3.6)	696 (4.8)	378 (2.4)
Blood pressure			
Systolic blood pressure — mmHg	126±17	129±16	123±18
Diastolic blood pressure — mmHg	78±11	79±10	77±11
Clinical chemistry			
Total cholesterol — mmol/L	5.5±1.1	5.3±1.1	5.6±1
HDL cholesterol — mmol/L	1.6±0.5	1.4±0.4	1.8±0.5
LDL cholesterol — mmol/L	3.4±1	3.4±1	3.5±1
Triglycerides — mmol/L	1.3±0.8	1.4±1	1.1±0.6
Glucose — mmol/L	5.8±1.1	6±1.2	5.6±1
HbA1c — mmol/mol	36.6±6.5	36.9±7.2	36.3±5.7
High-sensitivity C-reactive protein — mg/L	2.1±4.3	2.1±4.6	2.2±4.1
Estimated GFR — ml/min/1.73 m^2	85.1±12.1	85.7±11.7	84.5±12.4
Risk scores			
SCORE — %	1.4±1.3	2.1±1.4	0.7±0.6
PCE risk score — %	6.3±5.7	9.4±6.2	3.4±3.0
Prevalent cardiovascular disease			
Stroke — n (%)	465 (1.5)	263 (1.8)	202 (1.3)
Peripheral artery disease — n (%)	162 (0.5)	106 (0.7)	56 (0.4)
Heredity			
Family history of premature myocardial infarction — n (%)	2,012 (6.7)	883 (6.0)	1,129 (7.3)
Family history of premature stroke — n (%)	1,778 (5.9)	774 (5.3)	1,004 (6.5)

Plus-minus values are means ±SD. GFR, glomerular filtration rate. PCE, pooled cohort equation.

Supplemental Table II: Participation rate in SCAPIS per site, age and sex.

	Participants n (% of	Women n (% of participants)	Age groups, n (% of participants)		
			50-54 years	55-59 years	60-64 years
Gothenburg	6,265 (51.7)	3,276 (52.3)	2,058 (32.8)	2,128 (34.0)	2,079 (33.2)
Linköping	5,057 (58.0)	2,526 (50.0)	1,737 (34.3)	1,608 (31.8)	1,712 (33.9)
Malmö	6,251 (53.1)	3,322 (53.1)	2,057 (32.9)	2,081 (33.3)	2,113 (33.8)
Stockholm	5,038 (42.2)	2,517 (50.0)	1,749 (34.7)	1,664 (33.0)	1,625 (32.3)
Umeå	2,507 (54.5)	1,282 (51.1)	822 (32.8)	877 (35.0)	808 (32.2)
Uppsala	5,036 (46.8)	2,585 (51.3)	1,626 (32.3)	1,622 (32.2)	1,788 (35.5)
Total	**30,154 (50.3)**	**15,508 (51.4)**	**10,049 (33,3)**	**9,980 (33,1)**	**10,125 (33,6)**

59,909 subjects were randomly selected from the census register and contacted.

All percentages calculated within site.

Supplemental Table III: Characteristics of subjects who underwent CT but not CCTA.

Characteristic	SCAPIS	CT but not CCTA	CCTA sample
Sample size — n	30,154	2,228	25,182
Sociodemographics			
Men — n (%)	14,646 (48.6)	807 (36.2)	12,444
Age — years	57.5±4.4	58.2±4.3	57.4±4.3
Education, university degree — n (%)	13,218 (45.1)	880 (41.4)	11,263
Employed — n (%)	24,483 (81.2)	1,513 (67.9)	20,952
Anthropometry			
Body mass index at age 20 — kg/m^2	21.9±2.7	21.8±2.9	21.9±2.7
Body mass index — kg/m^2	27±4.5	27.6±5.6	26.8±4.3
Waist circumference — cm	94.4±13	95.1±15.2	94±12.6
Behavior			
Smoking status			
Current smoker — n (%)	3,728 (12.7)	309 (14.4)	3,079
Former smoker — n (%)	10,602 (36.0)	826 (38.4)	8,791
Mean pack years	7.5±12	8.7±13.1	7.2±11.7
Duration of smoking — years	11.8±15.6	13.5±16.5	11.6±15.4
Alcohol use			
Once per month or less — n (%)	7,198 (24.7)	764 (36.2)	5,649
2-4 times per month — n (%)	11,123 (38.1)	753 (35.6)	9,415
More than once a week — n (%)	10,865 (37.2)	596 (28.2)	9,452
Physical activity			
Time spent sedentary — % of active time	54±10.5	54.1±11.1	53.8±10.4
Time in moderate or vigorous activity — % of active time	6.4±3.4	6±3.5	6.4±3.4
Treatment			
Cholesterol-lowering medication — (%)	2,297 (7.6)	272 (12.2)	1,624 (6.4)
Antihypertensive medication — n (%)	5,768 (19.1)	636 (28.5)	4,437
Diabetes medication — n (%)	1,074 (3.6)	193 (8.7)	717 (2.8)
Blood pressure			
Systolic blood pressure — mmHg	126±17	126±18	126±17
Diastolic blood pressure — mmHg	78±11	77±11	78±10
Clinical chemistry			
Total cholesterol — mmol/L	5.5±1.1	5.5±1.1	5.5±1
HDL cholesterol — mmol/L	1.6±0.5	1.6±0.5	1.6±0.5
LDL cholesterol — mmol/L	3.4±1	3.4±1	3.5±1
Triglycerides — mmol/L	1.3±0.8	1.4±1.2	1.2±0.8
Glucose — mmol/L	5.8±1.1	6.1±1.8	5.7±1
HbA1c — mmol/mol	36.6±6.5	38.7±9.9	36.3±5.9
High-sensitivity C-reactive protein — mg/L	2.1±4.3	2.6±6.7	2.1±3.9
Estimated GFR — ml/min/1.73 m^2	85.1±12.1	80.5±17.3	85.4±11.5
Risk scores			
SCORE — %	1.4±1.3	1.3±1.3	1.4±1.3
PCE risk score — %	6.3±5.7	6.9±6.9	6.1±5.5
Prevalent cardiovascular disease			
Stroke — n (%)	465 (1.5)	59 (2.6)	343 (1.4)
Peripheral artery disease — n (%)	162 (0.5)	20 (0.9)	108 (0.4)
Heredity			
Family history of premature myocardial infarction — n (%)	2,012 (6.7)	153 (6.9)	1,619 (6.4)
Family history of premature stroke — n (%)	1,778 (5.9)	139 (6.2)	1,468 (5.8)

Plus–minus values are means ± SD. GFR, glomerular filtration rate. PCE, pooled cohort equation.

Supplemental Table IV: Reasons for not performing CCTA in subjects who underwent CT.

	Total		Men			Women	
		50-54 years	55-59 years	60-64 years	50-54 years	55-59 years	60-64 years
Subjects who did not undergo CCTA	2,228	214	260	329	397	493	531
Previous reaction to contrast media — n (%)	259 (11.6)	25 (11.7)	28 (10.8)	31 (9.4)	54 (13.6)	53 (10.8)	68 (12.8)
Renal impairment — n (%)	327 (14.7)	27 (12.6)	30 (11.5)	77 (23.4)	36 (9.1)	58 (11.8)	99 (18.6)
Venous access — n (%)	367 (16.5)	29 (13.6)	39 (15.0)	38 (11.6)	82 (20.7)	98 (19.9)	81 (15.3)
Subject declined CCTA — n (%)	521 (23.4)	52 (24.3)	53 (20.4)	49 (14.9)	108 (27.2)	129 (26.2)	128 (24.1)
Other reasons, total — n (%)	754 (33.8)	81 (37.9)	110 (42.3)	134 (40.7)	117 (29.5)	155 (31.4)	155 (29.2)
Adverse reaction to drugs	66 (8.8)	21 (25.9)	14 (12.7)	8 (6.0)	5 (4.3)	9 (5.8)	8 (5.2)
Allergy, other than contrast	63 (8.4)	8 (9.9)	8 (7.3)	8 (6.0)	7 (6.0)	20 (12.9)	12 (7.7)
Logistics (creatinine)*	82 (10.9)	3 (3.7)	9 (8.2)	7 (5.2)	18 (15.4)	19 (12.3)	26 (16.8)
Logistics (metformin)**	59 (7.8)	4 (4.9)	15 (13.6)	19 (14.2)	2 (1.7)	9 (5.8)	10 (6.5)
Logistics (study organization)	44 (5.8)	4 (4.9)	2 (1.8)	9 (6.7)	3 (2.6)	16 (10.3)	10 (6.5)
Thyroid disease	57 (7.6)	2 (2.5)	6 (5.5)	3 (2.2)	18 (15.4)	15 (9.7)	13 (8.4)
Other diseases	64 (8.5)	6 (7.4)	11 (10.0)	17 (12.7)	7 (6.0)	9 (5.8)	14 (9.0)
Language difficulties	90 (11.9)	13 (16.0)	13 (11.8)	15 (11.2)	20 (17.1)	15 (9.7)	14 (9.0)
Miscellaneous or unclear	229 (30.4)	20 (24.7)	32 (29.1)	48 (35.8)	37 (31.6)	43 (27.7)	48 (31.0)

*No access to p-creatinine before CCTA.

**Difficulties in postponing metformin treatment before CCTA.

Supplemental Table V: Missing data in participants in SCAPIS without established CHD who underwent successful CCTA (n=25,182).

Characteristic	Total
Sociodemographics	
Age — n (%)	0 (0)
Education, university degree — n (%)	589 (2.3)
Employed — n (%)	650 (2.6)
Anthropometry	
Body mass index at age 20 — n (%)	1,917 (7.6)
Body mass index — n (%)	0 (0.0)
Waist circumference — n (%)	8 (0.0)
Behavior	
***Smoking status (current/former)* — n (%)**	500 (2.0)
Mean pack years — n (%)	856 (3.4)
Duration of smoking — n (%)	46 (0.2)
***Alcohol use (complete AUDIT)* — n (%)**	804 (3.2)
***Physical activity (valid accelerometry)* — n (%)**	854 (3.4)
Treatment	
Cholesterol-lowering medication — n (%)	827 (3.3)
Antihypertensive medication — n (%)	825 (3.3)
Diabetes medication — n (%)	825 (3.3)
Blood pressure	
Systolic blood pressure — n (%)	6 (0.0)
Diastolic blood pressure — n (%)	4 (0.0)
Clinical chemistry	
Total cholesterol — n (%)	37 (0.1)
HDL cholesterol — n (%)	43 (0.2)
LDL cholesterol — n (%)	152 (0.6)
Triglycerides — n (%)	36 (0.1)
Glucose — n (%)	2,141 (8.5)
HbA1c — n (%)	83 (0.3)
High-sensitivity C-reactive protein — n (%)	36 (0.1)
Estimated GFR — n (%)	21 (0.1)
Risk scores	
SCORE —n (%)	41 (0.2)
Pooled Cohort Equation — n (%)	545 (2.2)
Prevalent cardiovascular disease	
Stroke — n (%)	815 (3.2)
Peripheral artery disease — n (%)	815 (3.2)
Heredity	
Family history of premature myocardial infarction — n (%)	596 (2.4)
Family history of premature stroke — n (%)	596 (2.4)

Supplemental Table VI. Inter- and intra-reader reproducibility for 10 coronary segments.

	Intra-agreement	Kappa	Inter-agreement	Kappa
Segment (5 grade*)	89	0.72 ± 0.03	89	0.67 ± 0.04
Segment (dichotomous)**	98	0.88 ± 0.04	96	0.77 ± 0.05
Five grade*				
LAD	92	0.85 ± 0.07	92	0.84 ± 0.07
CXA	90	0.63 ± 0.13	92	0.71 ± 0.11
RCA	98	0.92 ± 0.07	98	0.92 ± 0.08
Dichotomous**				
LAD	98	0.96 ± 0.14	96	0.91 ± 0.14
CXA	98	0.91 ± 0.14	100	1.00 ± 0.14
RCA	98	0.90 ± 0.14	94	0.72 ± 0.12
Subject (5 grade*)	88	0.78 ± 0.16	86	0.78 ± 0.08
Subject (dichotomous)**	96	0.91 ± 0.06	96	0.92 ± 0.06

Plus-minus values are means ±SD. Reading was done in 10 central segments (5, 6, 7, 11, 12, 13, 17, 1, 2, 3).

*The 5 grade analyses comprise: no atherosclerosis, 1-49% stenosis, ≥50% stenosis, calcium blooming, or technical artefact.

** The dichotomous analyses comprise: no atherosclerosis, any atherosclerosis (technical failures were coded as no atherosclerosis).

Supplemental Table VII: Technical failures and calcium blooming artefacts in the 11 central coronary vascular segments.

	Total		Men		Women	
	Technical failures	**Calcium blooming**	**Technical failures**	**Calcium blooming**	**Technical failures**	**Calcium blooming**
A. Subjects who completed CCTA (N=27,385)						
Sample size — n	27,385	27,385	13,618	13,618	13,767	13,767
Subject level	5,188 (18.9)	1,630 (6.0)	2,747 (20.2)	1,133 (8.3)	2,441 (17.7)	497 (3.6)
Left coronary artery	2,396 (8.7)	1,288 (4.7)	1,170 (8.6)	889 (6.5)	1,226 (8.9)	399 (2.9)
Left main	431 (1.6)	54 (0.2)	172 (1.3)	42 (0.3)	259 (1.9)	12 (0.1)
Proximal LAD	726 (2.7)	504 (1.8)	314 (2.3)	341 (2.5)	412 (3.0)	163 (1.2)
Mid LAD	1,136 (4.1)	725 (2.6)	560 (4.1)	502 (3.7)	576 (4.2)	223 (1.6)
Ramus intermedius	1,013 (3.7)	184 (0.7)	587 (4.3)	162 (1.2)	426 (3.1)	22 (0.2)
First diagonal	1,614 (6.1)	514 (1.9)	786 (6.0)	400 (3.0)	828 (6.2)	114 (0.8)
Circumflex artery	3,065 (11.2)	584 (2.1)	1,608 (11.8)	449 (3.3)	1,457 (10.6)	135 (1.0)
Proximal circumflex	899 (3.3)	253 (0.9)	406 (3.0)	180 (1.3)	493 (3.6)	73 (0.5)
Obtuse marginal 1	1,885 (6.9)	294 (1.1)	972 (7.1)	243 (1.8)	913 (6.6)	51 (0.4)
Mid and distal circumflex	2,099 (7.7)	202 (0.7)	1,066 (7.8)	166 (1.2)	1,033 (7.5)	36 (0.3)
Right coronary artery	2,607 (9.5)	432 (1.6)	1,270 (9.3)	307 (2.3)	1,337 (9.7)	125 (0.9)
Proximal RCA	928 (3.4)	190 (0.7)	433 (3.2)	138 (1.0)	495 (3.6)	52 (0.4)
Mid RCA	1,659 (6.1)	278 (1.0)	761 (5.6)	195 (1.4)	898 (6.5)	83 (0.6)
Distal RCA	1,389 (5.1)	157 (0.6)	673 (4.9)	132 (1.0)	716 (5.2)	25 (0.2)
B. Sample used to describe data on CCTA-detected atherosclerosis (n=25,182)						
Sample size — n	25,182	25,182	12,444	12,444	12,738	12,738
Subject level	3,206 (12.7)	1,309 (5.2)	1,742 (14.0)	892 (7.2)	1,464 (11.5)	417 (3.3)
Left coronary artery	1,103 (4.4)	1,041 (4.1)	577 (4.6)	705 (5.7)	526 (4.1)	336 (2.6)
Left main	0 (0.0)	30 (0.1)	0 (0.0)	23 (0.2)	0 (0.0)	7 (0.1)
Proximal LAD	0 (0.0)	389 (1.5)	0 (0.0)	250 (2.0)	0 (0.0)	139 (1.1)
Mid LAD	408 (1.6)	590 (2.3)	218 (1.8)	405 (3.3)	190 (1.5)	185 (1.5)
Ramus intermedius	612 (2.4)	134 (0.5)	384 (3.1)	116 (0.9)	228 (1.8)	18 (0.1)
First diagonal	842 (3.3)	403 (1.6)	430 (3.5)	309 (2.5)	412 (3.2)	94 (0.7)
Circumflex artery	1,702 (6.8)	441 (1.8)	938 (7.5)	331 (2.7)	764 (6.0)	110 (0.9)
Proximal circumflex	0 (0.0)	181 (0.7)	0 (0.0)	121 (1.0)	0 (0.0)	60 (0.5)
Obtuse marginal 1	964 (3.8)	227 (0.9)	537 (4.3)	186 (1.5)	427 (3.4)	41 (0.3)
Mid and distal circumflex	1,184 (4.7)	153 (0.6)	638 (5.1)	124 (1.0)	546 (4.3)	29 (0.2)
Right coronary artery	1,359 (5.4)	328 (1.3)	665 (5.3)	227 (1.8)	694 (5.4)	101 (0.8)
Proximal RCA	0 (0.0)	135 (0.5)	0 (0.0)	97 (0.8)	0 (0.0)	38 (0.3)
Mid RCA	873 (3.5)	211 (0.8)	404 (3.2)	145 (1.2)	469 (3.7)	66 (0.5)
Distal RCA	811 (3.2)	112 (0.4)	408 (3.3)	94 (0.8)	403 (3.2)	18 (0.1)

Data are n (%) of subjects with technical failures or calcium blooming.

Supplemental Table VIII: Characteristics of subjects with technical failures in any of the 4 most proximal segments.

Characteristic	Completed CCTA	Proximal segments technical failure	CCTA sample
Sample size — n	27,385	1,805	25,182
CCTA protocol used			
1	5,459 (19.9)	233 (12.9)	5,206 (20.7)
2	18,030 (65.8)	1,200 (66.5)	16,528 (65.6)
3	3,403 (12.4)	278 (15.4)	3,061 (12.2)
4A	336 (1.2)	50 (2.8)	278 (1.1)
4B	23 (0.1)	8 (0.4)	15 (0.1)
5	134 (0.5)	36 (2.0)	94 (0.4)
Pre-medication CCTA			
β-blocker — n (%)	19,929 (72.8)	1,181 (65.5)	18,502 (73.5)
Nitroprusside — n (%)	23,409 (85.5)	1,427 (79.1)	21,633 (85.9)
Pulse at CCTA	63.5±8.6	66.8±10.3	63.2±8.4
Sociodemographics			
Men — n (%)	13,618 (49.7)	863 (47.8)	12,444 (49.4)
Age — years	57.5±4.4	57.7±4.4	57.4±4.3
Anthropometry			
Body mass index — kg/m^2	26.9±4.4	28.4±5.2	26.8±4.3
Waist circumference — cm	94.4±12.7	98±13.9	94±12.6
Behavior			
Smoking status			
Current smoker — n (%)	3,341 (12.4)	203 (11.4)	3,079 (12.5)
Former smoker — n (%)	9,628 (35.9)	667 (37.6)	8,791 (35.6)
Treatment			
Cholesterol-lowering medication — (%)	1,999 (7.3)	204 (11.3)	1,624 (6.4)
Antihypertensive medication — n (%)	5,056 (18.5)	438 (24.3)	4,437 (17.6)
Diabetes medication — n (%)	868 (3.2)	100 (5.5)	717 (2.8)
Blood pressure			
Systolic blood pressure — mmHg	126±17	126±17	126±17
Diastolic blood pressure — mmHg	78±10	78±11	78±10
Clinical chemistry			
Total cholesterol — mmol/L	5.5±1.1	5.4±1.1	5.5±1
HDL cholesterol — mmol/L	1.6±0.5	1.6±0.5	1.6±0.5
LDL cholesterol — mmol/L	3.4±1	3.4±1	3.5±1
Triglycerides — mmol/L	1.2±0.8	1.3±0.9	1.2±0.8
Glucose — mmol/L	5.7±1.1	5.9±1.3	5.7±1
HbA1c — mmol/mol	36.4±6.1	37.5±8	36.3±5.9
High-sensitivity C-reactive protein — mg/L	2.1±3.9	2.4±4.1	2.1±3.9
Estimated GFR — ml/min/1.73 m^2	85.4±11.5	85.3±11.8	85.4±11.5
Risk scores			
SCORE — %	1.4±1.3	1.4±1.3	1.4±1.3
PCE risk score — %	6.3±5.6	6.8±6.3	6.1±5.5
Prevalent cardiovascular disease			
Stroke — n (%)	392 (1.4)	33 (1.8)	343 (1.4)
Peripheral artery disease — n (%)	141 (0.5)	23 (1.3)	108 (0.4)
Heredity			
Family history of premature MI — n (%)	1,822 (6.7)	148 (8.2)	1,619 (6.4)
Family history of premature stroke — n	1,619 (5.9)	117 (6.5)	1,468 (5.8)

Plus–minus values are means ±SD. GFR, glomerular filtration rate. PCE, pooled cohort equation.

Supplemental Table IX: Prevalence of atherosclerosis in the SCAPIS cohort after adjustment to age-matched populations using IPPW.

Characteristic	Unweighted*	Standardized to catchment area population 50-64 years	Standardized to national population 50-64 years
No atherosclerosis	57.9 (57.3-58.5)	57.9 (57.3-58.5)	57.2 (56.2-58.3)
Any form of atherosclerosis	42.1 (41.5-42.7)	42.1 (41.4-42.7)	42.7 (41.7-43.8)
Any stenosis ≥50%	5.2 (5.0-5.5)	5.3 (5.0-5.6)	6.2 (5.7-6.9)
One vessel disease	4.3 (4.0-4.5)	4.3 (4.0-4.6)	5.0 (4.5-5.5)
Two vessel disease	0.8 (0.7-0.9)	0.8 (0.7-0.9)	1.1 (0.8-1.4)
Three vessel disease	0.2 (0.1-0.3)	0.2 (0.1-0.2)	0.2 (0.1-0.3)
Left main disease	0.1 (0.1-0.2)	0.1 (0.1-0.2)	0.2 (0.1-0.3)
Proximal LAD disease	1.9 (1.7-2.0)	1.8 (1.7-2.0)	2.2 (1.8-2.6)
Left main, proximal LAD or three-vessel disease	1.9 (1.8-2.1)	1.9 (1.8-2.1)	2.3 (1.9-2.7)
Segment involvement score ≥4%	11.9 (11.5-12.3)	11.9 (11.5-12.3)	12.8 (12.1-13.6)
Only non-calcified plaques	2.4 (2.2-2.6)	2.5 (2.3-2.7)	2.5 (2.2-2.8)
Any plaque non-calcified	8.3 (8.0-8.7)	8.4 (8.0-8.8)	8.7 (8.1-9.4)
Any non-calcified stenosis ≥50%	1.2 (1.1-1.4)	1.3 (1.1-1.4)	1.3 (1.1-1.7)

Values are percentages with 95% robust binomial confidence intervals in parentheses that account for the sampling weights.

*Analysis sample (n = 25,182).

Supplemental Table X: Prevalence of atherosclerosis in the SCAPIS cohort when calcium blooming was defined as ≥50% stenosis.

Characteristic	Total	Men			Women		
		50-54 years	55-59 years	60-64 years	50-54 years	55-59 years	60-64 years
No atherosclerosis — n (%)	14,579 (57.9)	2,516 (58.8)	1,791 (43.4)	1,262 (31.3)	3,532 (81.2)	2,960 (70.7)	2,518 (59.9)
Any form of atherosclerosis — n (%)	10,603 (42.1)	1,762 (41.2)	2,337 (56.6)	2,776 (68.7)	816 (18.8)	1,229 (29.3)	1,683 (40.1)
Any stenosis ≥50% — n (%)	2,340 (9.3)	308 (7.2)	522 (12.6)	875 (21.7)	119 (2.7)	192 (4.6)	324 (7.7)
One vessel disease — n (%)	1,652 (6.6)	233 (5.4)	359 (8.7)	580 (14.4)	95 (2.2)	146 (3.5)	239 (5.7)
Two vessel disease — n (%)	446 (1.8)	52 (1.2)	107 (2.6)	179 (4.4)	20 (0.5)	31 (0.7)	57 (1.4)
Three vessel disease — n (%)	242 (1.0)	23 (0.5)	56 (1.4)	116 (2.9)	4 (0.1)	15 (0.4)	28 (0.7)
Left main disease — n (%)	65 (0.3)	5 (0.1)	12 (0.3)	31 (0.8)	2 (0.0)	5 (0.1)	10 (0.2)
Proximal LAD disease — n (%)	859 (3.4)	95 (2.2)	190 (4.6)	328 (8.1)	45 (1.0)	69 (1.6)	132 (3.1)
Left main, proximal LAD or three-vessel disease — n (%)	935 (3.7)	107 (2.5)	207 (5.0)	359 (8.9)	46 (1.1)	78 (1.9)	138 (3.3)
Segment involvement score ≥4 — n (%)	3,003 (11.9)	424 (9.9)	753 (18.2)	1,182 (29.3)	93 (2.1)	201 (4.8)	350 (8.3)
Only non-calcified plaques — n (%)	607 (2.4)	117 (2.7)	107 (2.6)	94 (2.3)	100 (2.3)	96 (2.3)	93 (2.2)
Any plaque non-calcified — n (%)	2,102 (8.3)	359 (8.4)	492 (11.9)	575 (14.2)	160 (3.7)	224 (5.3)	292 (7.0)
Any non-calcified stenosis ≥50% — n (%)	315 (1.3)	42 (1.0)	80 (1.9)	110 (2.7)	16 (0.4)	24 (0.6)	43 (1.0)

Supplemental Table XI. Distribution of CCTA-detected atherosclerosis in the 11 most proximal coronary segments in men and women divided by age group in the SCAPIS cohort (n=25,182).

50-54 years of age

	Men (denominator 4,278)				Women (denominator 4,348)		
Segment	**Any stenosis ≥50%**	**Only stenosis 1-49%**	**Any form of atherosclerosis**	**Segment**	**Any stenosis ≥50%**	**Only stenosis 1-49%**	**Any form of atherosclerosis**
s01	14 (0.3%)	376 (8.8%)	390 (9.1%)	**s01**	2 (0%)	127 (2.9%)	129 (3%)
s02	17 (0.4%)	393 (9.2%)	410 (9.6%)	**s02**	6 (0.1%)	129 (3%)	135 (3.1%)
s03	7 (0.2%)	238 (5.6%)	245 (5.7%)	**s03**	2 (0%)	62 (1.4%)	64 (1.5%)
s04	6 (0.1%)	6 (0.1%)	12 (0.3%)	**s04**	0 (0%)	0 (0%)	0 (0%)
s05	4 (0.1%)	306 (7.2%)	310 (7.2%)	**s05**	1 (0%)	118 (2.7%)	119 (2.7%)
s06	62 (1.4%)	1129 (26.4%)	1191 (27.8%)	**s06**	18 (0.4%)	497 (11.4%)	515 (11.8%)
s07	80 (1.9%)	812 (19%)	892 (20.9%)	**s07**	19 (0.4%)	288 (6.6%)	307 (7.1%)
s08	4 (0.1%)	5 (0.1%)	9 (0.2%)	**s08**	0 (0%)	2 (0%)	2 (0%)
s09	30 (0.7%)	225 (5.3%)	255 (6%)	**s09**	6 (0.1%)	59 (1.4%)	65 (1.5%)
s10	3 (0.1%)	9 (0.2%)	12 (0.3%)	**s10**	0 (0%)	5 (0.1%)	5 (0.1%)
s11	11 (0.3%)	382 (8.9%)	393 (9.2%)	**s11**	2 (0%)	130 (3%)	132 (3%)
s12	8 (0.2%)	149 (3.5%)	157 (3.7%)	**s12**	0 (0%)	38 (0.9%)	38 (0.9%)
s13	16 (0.4%)	133 (3.1%)	149 (3.5%)	**s13**	1 (0%)	31 (0.7%)	32 (0.7%)
s14	1 (0%)	6 (0.1%)	7 (0.2%)	**s14**	0 (0%)	2 (0%)	2 (0%)
s15	0 (0%)	1 (0%)	1 (0%)	**s15**	0 (0%)	1 (0%)	1 (0%)
s16	1 (0%)	1 (0%)	2 (0%)	**s16**	0 (0%)	0 (0%)	0 (0%)
s17	5 (0.1%)	105 (2.5%)	110 (2.6%)	**s17**	4 (0.1%)	13 (0.3%)	17 (0.4%)
s18	0 (0%)	0 (0%)	0 (0%)	**s18**	0 (0%)	0 (0%)	0 (0%)

55-59 years of age

	Men (denominator 4,128)				Women (denominator 4,189)		
Segment	**Any stenosis ≥50%**	**Only stenosis 1-49%**	**Any form of atherosclerosis**	**Segment**	**Any stenosis ≥50%**	**Only stenosis 1-49%**	**Any form of atherosclerosis**
s01	37 (0.9%)	629 (15.2%)	666 (16.1%)	**s01**	5 (0.1%)	252 (6%)	257 (6.1%)
s02	43 (1%)	572 (13.9%)	615 (14.9%)	**s02**	15 (0.4%)	210 (5%)	225 (5.4%)
s03	28 (0.7%)	366 (8.9%)	394 (9.5%)	**s03**	3 (0.1%)	102 (2.4%)	105 (2.5%)
s04	6 (0.1%)	13 (0.3%)	19 (0.5%)	**s04**	1 (0%)	3 (0.1%)	4 (0.1%)
s05	6 (0.1%)	558 (13.5%)	564 (13.7%)	**s05**	3 (0.1%)	216 (5.2%)	219 (5.2%)
s06	111 (2.7%)	1585 (38.4%)	1696 (41.1%)	**s06**	29 (0.7%)	790 (18.9%)	819 (19.6%)

s07	137 (3.3%)	1111 (26.9%)	1248 (30.2%)	**s07**	31 (0.7%)	474 (11.3%)	505 (12.1%)
s08	5 (0.1%)	10 (0.2%)	15 (0.4%)	**s08**	0 (0%)	2 (0%)	2 (0%)
s09	58 (1.4%)	349 (8.5%)	407 (9.9%)	**s09**	6 (0.1%)	110 (2.6%)	116 (2.8%)
s10	6 (0.1%)	13 (0.3%)	19 (0.5%)	**s10**	1 (0%)	6 (0.1%)	7 (0.2%)
s11	27 (0.7%)	552 (13.4%)	579 (14%)	**s11**	6 (0.1%)	249 (5.9%)	255 (6.1%)
s12	25 (0.6%)	244 (5.9%)	269 (6.5%)	**s12**	2 (0%)	61 (1.5%)	63 (1.5%)
s13	17 (0.4%)	212 (5.1%)	229 (5.5%)	**s13**	4 (0.1%)	57 (1.4%)	61 (1.5%)
s14	3 (0.1%)	7 (0.2%)	10 (0.2%)	**s14**	0 (0%)	2 (0%)	2 (0%)
s15	1 (0%)	2 (0%)	3 (0.1%)	**s15**	1 (0%)	1 (0%)	2 (0%)
s16	3 (0.1%)	6 (0.1%)	9 (0.2%)	**s16**	0 (0%)	2 (0%)	2 (0%)
s17	26 (0.6%)	142 (3.4%)	168 (4.1%)	**s17**	1 (0%)	28 (0.7%)	29 (0.7%)
s18	0 (0%)	0 (0%)	0 (0%)	**s18**	0 (0%)	1 (0%)	1 (0%)

60-65 years of age

	Men (denominator 4,038)				**Women (denominator 4,200)**		
Segment	**Any stenosis ≥50%**	**Only stenosis 1-49%**	**Any form of atherosclerosis**	**Segment**	**Any stenosis ≥50%**	**Only stenosis 1-49%**	**Any form of atherosclerosis**
s01	53 (1.3%)	955 (23.7%)	1008 (25%)	**s01**	20 (0.5%)	382 (9.1%)	402 (9.6%)
s02	62 (1.5%)	861 (21.3%)	923 (22.9%)	**s02**	16 (0.4%)	357 (8.5%)	373 (8.9%)
s03	36 (0.9%)	580 (14.4%)	616 (15.3%)	**s03**	8 (0.2%)	156 (3.7%)	164 (3.9%)
s04	7 (0.2%)	21 (0.5%)	28 (0.7%)	**s04**	4 (0.1%)	6 (0.1%)	10 (0.2%)
s05	15 (0.4%)	848 (21%)	863 (21.4%)	**s05**	6 (0.1%)	342 (8.1%)	348 (8.3%)
s06	176 (4.4%)	1962 (48.6%)	2138 (52.9%)	**s06**	50 (1.2%)	1157 (27.5%)	1207 (28.7%)
s07	223 (5.5%)	1476 (36.6%)	1699 (42.1%)	**s07**	53 (1.3%)	659 (15.7%)	712 (17%)
s08	11 (0.3%)	16 (0.4%)	27 (0.7%)	**s08**	0 (0%)	4 (0.1%)	4 (0.1%)
s09	88 (2.2%)	507 (12.6%)	595 (14.7%)	**s09**	19 (0.5%)	152 (3.6%)	171 (4.1%)
s10	11 (0.3%)	33 (0.8%)	44 (1.1%)	**s10**	4 (0.1%)	10 (0.2%)	14 (0.3%)
s11	48 (1.2%)	918 (22.7%)	966 (23.9%)	**s11**	9 (0.2%)	398 (9.5%)	407 (9.7%)
s12	39 (1%)	397 (9.8%)	436 (10.8%)	**s12**	4 (0.1%)	113 (2.7%)	117 (2.8%)
s13	25 (0.6%)	320 (7.9%)	345 (8.5%)	**s13**	6 (0.1%)	106 (2.5%)	112 (2.7%)
s14	5 (0.1%)	7 (0.2%)	12 (0.3%)	**s14**	0 (0%)	3 (0.1%)	3 (0.1%)
s15	0 (0%)	3 (0.1%)	3 (0.1%)	**s15**	0 (0%)	0 (0%)	0 (0%)
s16	4 (0.1%)	4 (0.1%)	8 (0.2%)	**s16**	1 (0%)	4 (0.1%)	5 (0.1%)
s17	27 (0.7%)	219 (5.4%)	246 (6.1%)	**s17**	3 (0.1%)	53 (1.3%)	56 (1.3%)
s18	1 (0%)	2 (0%)	3 (0.1%)	**s18**	0 (0%)	0 (0%)	0 (0%)

Supplemental Table XII: Characteristics of participants in SCAPIS without established CHD who underwent both successful CCTA and CAC scoring (n=25,014), divided by zero or positive CAC and absence or presence of CCTA-detected atherosclerosis.

	CAC = 0		CAC >0	
Characteristic	**CCTA-**	**CCTA+**	**CCTA-**	**CCTA+**
Sample size — n	14,139	818	367	9690
Sociodemographics				
Sex, women — n (%)	8,807 (62.3)	400 (48.9)	154 (42.0)	3,305 (34.1)
Age — years	56.6±4.3	57.1±4.3	57.4±4.3	58.6±4.2
Education, university degree — n (%)	6,757 (48.8)	363 (45.3)	135 (38.4)	3,942 (41.8)
Employed — n (%)	12,122 (85.7)	666 (81.4)	297 (80.9)	7725 (79.7)
Anthropometry				
Body mass index at age 20 — kg/m^2	21.6±2.6	21.9±2.7	22.3±2.6	22.4±2.7
Body mass index — kg/m^2	26.3±4.2	27.4±4.1	27.7±4.4	27.4±4.3
Waist circumference — cm	91.6±12.3	95.5±11.8	96.4±12.5	97.2±12.4
Behavior				
Smoking status				
Current smoker — n (%)	1,445 (10.4)	105 (13.1)	36 (10.2)	1,482 (15.7)
Former smoker — n (%)	4,613 (33.2)	273 (34.0)	119 (33.8)	3,716 (39.2)
Mean pack years	5.7±10.1	7.2±11.7	6.4±11.7	9.4±13.4
Duration of smoking — years	9.8±14.2	11.6±15.4	10.1±15.1	14.2±16.7
Alcohol use				
Once per month or less — n (%)	3,246 (23.5)	226 (28.3)	91 (26.0)	2,054 (21.9)
2-4 times per month — n (%)	5,349 (38.7)	283 (35.4)	150 (42.9)	3,564 (38.0)
More than once a week — n (%)	5,234 (37.8)	290 (36.3)	109 (31.1)	3,765 (40.1)
Physical activity				
Time spent sedentary — % of active time	53.3±10.2	55.0±10.4	55.8±10.1	54.4±10.5
Time in moderate or vigorous activity — % of active time	6.5±3.3	6.3±3.6	6.3±3.2	6.4±3.5
Treatment				
Cholesterol-lowering medication — (%)	498 (3.5)	36 (4.4)	24 (6.5)	1,053 (10.9)
Antihypertensive medication — n (%)	1,736 (12.3)	154 (18.8)	71 (19.3)	2,441 (25.2)
Diabetes medication — n (%)	215 (1.5)	19 (2.3)	11 (3.0)	469 (4.8)
Blood pressure				
Systolic blood pressure — mmHg	123±17	128±17	131±17	129±16

Diastolic blood pressure — mmHg	76±10	79±11	82±11	79±10
Clinical chemistry				
Total cholesterol — mmol/L	5.5±1.0	5.6±1.1	5.6±1.1	5.6±1.1
HDL cholesterol — mmol/L	1.7±0.5	1.6±0.5	1.5±0.5	1.5±0.5
LDL cholesterol — mmol/L	3.4±0.9	3.6±0.9	3.5±0.9	3.6±1.0
Triglycerides — mmol/L	1.1±0.7	1.3±0.8	1.3±0.7	1.4±0.9
Glucose — mmol/L	5.6±0.8	5.7±0.9	5.7±0.8	5.9±1.3
HbA1c — mmol/mol	35.6±4.7	36.2±6.3	36.3±5.6	37.2±7.1
High-sensitivity C-reactive protein — mg/L	1.9±3.5	2.3±4.4	1.9±2.1	2.2±4.4
Estimated GFR — ml/min/1.73 m^2	85±12	86±11	84±11	86±11
Risk scores				
SCORE — %	1.0±1.0	1.4±1.3	1.6±1. 5	1.9±1.5
PCE — %	4.6±4.1	6.5±5.5	6.9±5.3	8.6±6.3
Prevalent cardiovascular disease				
Stroke — n (%)	147 (1.0)	11 (1.3)	2 (0.5)	181 (1.9)
Peripheral artery disease — n (%)	31 (0.2)	1 (0.1)	0 (0.0)	76 (0.8)
Heredity				
Family history of premature myocardial infarction — n (%)	799 (5.7)	51 (6.2)	27 (7.4)	731 (7.5)
Family history of premature stroke — n (%)	762 (5.4)	51 (6.2)	29 (7.9)	616 (6.4)

Plus-minus values are means ±SD. GFR, glomerular filtration rate. PCE, pooled cohort equation.

Supplemental Table XIII. Odds ratios (95% confidence intervals) for risk factors associated with discrepancies between CCTA-detected atherosclerosis and CAC scores in participants in SCAPIS without established CHD who underwent both successful CCTA and CAC scoring.

Characteristic	CCTA+ (n=818) in the population with zero CAC (n=14,957)	CAC >0 (n=367) in the population without CCTA-detected atherosclerosis (n=14,506)
Sample size (complete case analyses) — n	14,679	14,228
Sociodemographics		
Sex (male)	1.48 (1.259, 1.739)	1.902 (1.494, 2.421)
Age (per year)	1.021 (1.004, 1.039)	1.034 (1.007, 1.06)
Anthropometry		
Obesity (body mass index >30)	1.252 (1.045, 1.5)	1.331 (1.025, 1.73)
Smoking status		
Current smoker	1.264 (1.019, 1.568)	0.993 (0.697, 1.413)
Treatment		
Cholesterol-lowering medication	1.074 (0.744, 1.55)	1.522 (0.961, 2.41)
Antihypertensive medication	1.383 (1.135, 1.687)	1.222 (0.914, 1.635)
Diabetes, self report	0.946 (0.665, 1.345)	1.247 (0.801, 1.941)
Blood pressure		
Systolic blood pressure (per mmHg)	1.01 (1.005, 1.014)	1.018 (1.011, 1.024)
Clinical chemistry		
Total cholesterol (per mmol/L)	1.222 (1.138, 1.313)	1.159 (1.04, 1.29)
HDL cholesterol (per mmol/L)	0.642 (0.536, 0.768)	0.674 (0.514, 0.884)

Odds ratios are calculated per unit change for continuous variables.