Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Information on cohorts

Original cohorts:

The Framingham Heart Study

The Framingham Heart Study (FHS) began in 1948 with the enrollment of 5,209 men and women, 28 to 62 years of age. Participants underwent physical examinations every 2 years.[1,2] In 1971, 5,124 participants were enrolled, mainly consisting of children of the Original FHS cohort and the children's spouses were enrolled (the Offspring cohort).[3,4] The Third Generation cohort began in 2002 when 4,095 children of the Offspring cohort participants were enrolled.[5] Participants in the Offspring and Third Generation cohorts were invited to enroll in the multidetector computed tomographic (MDCT) substudy. A total of 3,529 participants (1,418 from Offspring, 2,111 from Third Generation) underwent MDCT scanning to measure their coronary artery calcium (CAC) between 2002 and 2005. To be eligible for the study, participants were required to weigh <160 kg because of MDCT scanner specifications, to be ≥35 years of age if a man or ≥40 years of age if a woman, and nonpregnant.[6] The original data collection protocols were approved by the institutional review boards at Boston University and Massachusetts General Hospital, Boston, Massachusetts, and written informed consent was obtained from all participants. The MDCT substudy protocol was reviewed by the Tufts University institutional review board.

At each follow-up examination, FHS participants underwent a routine physical examination, medical history interview, and fasting laboratory tests, including total cholesterol and high-density lipoprotein cholesterol (HDL-C), and fasting glucose. In this study, traditional risk factors were assessed at the 7th Offspring examination (1998 to 2001), occurring approximately 4 years before the MDCT substudy, and at the first examination of the Third Generation cohort (2002 to 2005), occurring contemporaneously with the MDCT substudy. Blood pressure (BP) was measured twice by a physician and averaged to calculate systolic BP (SBP) and diastolic BP (DBP), respectively. Hypertension was defined as SBP≥140 mm Hg, DBP≥90 mm Hg, or antihypertensive medication use. Diabetes mellitus was defined as a fasting plasma glucose level ≥126 mg/dl or antihyperglycemic medication use. Current smoking was defined by having smoked ≥1 cigarette/day for the previous year.

Between 2002 and 2005, participants underwent imaging on an 8-slice MDCT scanner (LightSpeed Ultra; General Electric, Milwaukee, Wisconsin) with prospective

electrocardiographic triggering, during a single breath hold in midinspiration (typically 18 seconds) using sequential data acquisition.[6] Scans were prospectively initiated at 50% of the RR interval, which has been widely used for MDCT-based measurements of CAC and has been shown to provide the best average image quality for MDCT-based data acquisition.[7] Forty-eight contiguous 2.5-mm-thick slices (120 kVp, 320 or 400 mA for <220 and >220 pounds of body weight, respectively), and gantry rotation time and temporal resolution 500ms) were acquired. Effective radiation exposure was 1.0 to 1.25 mSv for 320 and 400 mA, respectively. Using a dedicated offline workstation (Aquarius, Terarecon, San Mateo, California), an experienced reader assessed the presence and amount of CAC. A calcified lesion was identified as an area of ≥3 connected pixels of attenuation >130 Hounsfield units applying 3-dimentional connectivity criteria (6 points). Agatston score was calculated by calculated by multiplying the area of each lesion with a weighted attenuation score dependent on the maximal attenuation within the lesion.[8]

Participants were contacted annually for telephone follow-up. For this study, the final date of follow-up was December 31, 2013. If a participant reported that he/she saw a physician, visited an emergency department, or was admitted to the hospital, all medical records from practitioners, hospitals, imaging centers, rehabilitation centers, and nursing homes were procured for review. This information included medical histories, physical examinations at the study clinic, hospitalization records, and communication with personal physicians.[9] All atherosclerotic cardiovascular disease (ASCVD) events were adjudicated using standardized criteria by an end-point committee of 3 senior investigators using the same criteria and all available medical records (https://www.framinghamheartstudy.org/). Coronary heart disease (CHD) included myocardial infarction (diagnostic ECG, cardiac biomarkers, and clinical presentation) and CHD deaths. Stroke cases were reviewed and adjudicated by a panel of study neurologists.

The Multi-Ethnic Study of Atherosclerosis

The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective, population-based cohort, comprising 4 prespecified ethnicities (white, African American, Hispanic, and Chinese) and 6 US communities (Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; New York, New York; and St Paul, Minnesota).[10] The primary goal of the MESA study is to evaluate the characteristics and risk factors of (subclinical) cardiovascular diseases. A total of 6,809 participants ages 45-84 years without cardiovascular diseases at baseline

were recruited from July 2000 through September 2002, and CAC scoring was conducted at baseline. The MESA study was approved by the institutional review boards of each study site and written informed consent was obtained from all participants.

In the MESA, a questionnaire was used to obtain demographic data, cardiovascular risk factors, and medical history between 2000 and 2002. Resting BP was measured 3 times with participants being in a seated position, using a Dinamap model Pro100 automated oscillometric sphygmomanometer (Critikon). The mean of the last 2 measurements was used in analysis. Total cholesterol, HDL-C, and plasma glucose levels were measured after a 12-hour fast. Hypertension was defined as a BP of 140/90 mm Hg or higher, self-reported hypertension confirm by antihypertensive medication use. Diabetes mellitus was defined as a fasting glucose level of 126 mg/dL or higher, or antihyperglycemic medication use. Current smoking was defined as having smoked a cigarette in the last 30 days.

The MESA CAC scanning protocol has been previously described.[11] Each of the six centers conducted CAC measures with either a cardiac-gated electron-beam CT scanner (Chicago, Los Angeles, New York) or a MDCT (Baltimore, Forsyth County, St. Paul) acquired at 50% of the R-R interval. All participants were scanned twice with mean CAC (Agatston) score used for all analyses.[8] Estimates of radiation dose, determined according to the MESA protocol for a single scan obtained through the heart, with the Imatron C150, Volume Zoom, and LightSpeed Pro 16 scanners were as follows: 0.6 and 0.7, 0.9 and 1.1, and 0.9 and 1.1 mSv for men and women, respectively.[12] Images were interpreted at the MESA CT reading center (Los Angeles Biomedical Research Institute at Harbor-University of California Los Angeles, Torrance, CA, USA). The intra- and inter-observer agreements were $\kappa = 0.93$ and 0.90, respectively. Calcified plaques were defined as CT attenuation of ≥130 Hounsfield Units (HU), 4 contiguous pixels (1.86 mm^2 for 4-detector-row CT; 1.83 mm^2 for electron-beam CT), and location within an 8-mm radius of the coronary artery trajectory.

At intervals of 9-12 months, an interviewer contacted each participant or family member by telephone to inquire about interim hospital admissions, outpatient diagnoses of ASCVD, and deaths (http://www.mesa-nhlbi.org/).[10] For this study, the final date of follow-up was December 31, 2011. Two physicians from the MESA mortality and morbidity review committee independently ascertained events. In the event of disagreement, the full committee made the final classification. CHD events included

myocardial infarction and CHD deaths. The diagnosis of MI was based on a combination of symptoms, electrocardiographic findings, and levels of cardiac biomarkers. We used hospital records and family interviews to determine whether deaths were related to CHD. A death was considered related to CHD if it occurred within 28 days after a myocardial infarction, if the participant had had chest pain within the 72 h before death or if the participant had a history of CHD and there was no known non-atherosclerotic, non-cardiac cause of deaths. Stroke was defined as a rapid onset of neurologic deficit, headache, or meningismus, and neurologic deficits not secondary to brain trauma, tumor, infection, or other non-vascular cause, and clinically relevant lesion on brain imaging, duration greater than 24 hours, or death within 24 hours.

The Cardiovascular Health Study

The Cardiovascular Health Study (CHS) is a population-based, longitudinal cohort study established in 1989, recruited those aged ≥65 years from 4 US metropolitan communities: Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh, Pennsylvania. The design for the CHS has been described previously.[13,14]

The primary goal of the CHS is to determine cardiovascular risk factors associated with cardiovascular disease event in older adults. An initial cohort of 5,201 predominantly white individuals was recruited in 1989-1990 (original cohort), and an additional cohort of 687 African American individuals was recruited in 1992–1993 (supplemental cohort). Between 1998 and 2000, 614 (84%) of 727 participants who visited in Pittsburgh, Pennsylvania at the final examination underwent electron beam tomography scanning.[15,16] Nonparticipants were too ill or could not travel (61%), had died after the last clinic visit (16%), or refused (23%). All participants gave informed consent for the protocol, which was approved by the Institutional Review Board of the University of Pittsburgh.

Cardiovascular risk factors were assessed at the 1998 or 1999 clinical examination. Participants self-reported age, sex, race, smoking history, and medication use, using a validated medication inventory. Participants were asked to fast for 8 to 12 hours overnight prior to the study visit. Trained research staff took 3 seated BP readings, using a standard mercury sphygmomanometer. The average of the last 2 readings was used for the analysis. Hypertension was defined as a BP of 140/90 mm Hg or higher, or self-reported hypertension confirmed by antihypertensive medication use. Diabetes mellitus

was defined as a fasting glucose level of 126 mg/dL or higher, or self-reported diabetes confirmed by antihyperglycemic medication use. Cigarette smoking was analyzed as current use or not (never and past smoking).

Electron-beam CT (Imatron C-150 scanner, San Francisco, California) was used to assess CAC, using a base value region of interest computer program that extracts all pixels with 130 Hounsfield units within an operator-defined region of interest in each 3-mm-thick image of the coronary arteries (26 cm^2 field of view).[13,14] All pixels >130 Hounsfield units and >1 mm (≥2 contiguous pixels) within the coronary arteries were considered to be calcium. The calcium score was calculated for each region by multiplying the area of significant pixels by a grade number (1, 2, 3, or 4) indicative of the peak computed tomographic number (Hounsfield units). The individual region of interest scores were then summed for a total CAC (Agatston) score.[8]

Participants were interviewed by telephone or during an annual in-person clinical examination every 6 months to ascertain incident ASCVD events (https://chs-nhlbi.org/).[13] For this study, the final date of follow-up was June 2009. The related medical records and informant interviews were reviewed by a central morbidity and mortality committee to confirm fatal and nonfatal ASCVD events including CHD and stroke. CHD included myocardial infarction, or CHD death. Incident stroke was ascertained by self-report or from the Health Care Financing Administration hospitalized patient database of International Classification of Diseases, 9th Revision (ICD-9) codes. For confirmation of stroke, hospital records, including cranial computed tomography and cerebral magnetic resonance images, were reviewed by a committee that included neurologists and a neuroradiologist.

Confirmation cohorts:

The Rotterdam Study

The Rotterdam Study is a prospective population-based cohort study, recruiting participants≥55 years of age from 1990 (original Cohort, Rotterdam Study-I). Starting in 2000, the original cohort was extended with a second cohort of subjects who reached 55 years of age and those who had moved to the research area (Rotterdam Study-II). The rationale and design of the Rotterdam Study were described elsewhere.[17] Rotterdam Study participants are visited every 3-5 years in the research center. For the current study, we used data from the third examination of the original cohort (Rotterdam Study-I, visit

3) and the second examination of the extended cohort (Rotterdam Study-II visit 2) who underwent coronary calcium scan. For the present analysis, we further excluded those< 60 years of age; those with known CHD, stroke, and HF at baseline; those who had any missing covariates required for the current analyses; and those lost to follow-up. A total of 3,089 participants were included in this study. The study was approved by the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam, the Netherlands. All participants provided written informed consent to participate in the study and to obtain information from their treating physicians separately.

BP was measured at the right brachial artery with a random-zero sphygmomanometer with the participant in sitting position. The mean of 2 consecutive measurements was used for the analysis. Hypertension was defined as a BP of 140/90 mm Hg or higher, or antihypertensive medication use with indication for hypertension. After an overnight fast, blood samples were obtained at the research center. Serum total cholesterol, HDL-C, and glucose were measured using standard techniques. Diabetes mellitus was defined as a fasting glucose level of 126 mg/dL or higher, or antihyperglycemic medication use. Information on smoking was obtained during the home interview of the Rotterdam Study, and analyzed as current use or not (never and past smoking).

Assessment of CAC score was performed with an electron-beam CT C-150 Imatron scanner (GE-Imatron Inc., South San Francisco, California) in the third examination of the original cohort (Rotterdam Study-I visit 3) or with a 16-slice or 64-slice MDCT scanners (SOMATON Sensation 16 or 64, Siemens, Forcheim, Germany) in the second examination of the extended cohort (Rotterdam Study-II visit 2).[18,19] For the electron-beam CT scan, from the level of the root of the aorta through the heart, 38 images were obtained with 100-ms scan time and 3-mm slice thickness. Using ECG triggering, we acquired images at 80% of the cardiac cycle during a single breathhold. CAC score was measured with AccuImage software (AccuImage Diagnostics Corp), displaying all pixels with a density >130 Hounsfield units. A calcification was defined as a minimum of 2 adjacent pixels (area, 0.65 mm^2) with a density >130 Hounsfield units. Calcium scores were calculated according to Agatston's method.[8] Scans were read by two trained readers, one of whom is an experienced radiologist. The scan readers were blinded to the clinical data of the participants.[18] For the MDCT scan, the cardiac scan reached from the apex of the heart to the tracheal bifurcation. Atherosclerotic calcification was identified based on a threshold of 130 HU, using dedicated software (Syngo Calcium Scoring, Siemens, Forcheim, Germany). Calcification was quantified by using the Agatston score. The total

score per vascular bed was calculated by adding the scores of all lesions in that bed. The estimated radiation dose was up to 2.1 millisievert (mSv) for the cardiac scan. In the minority of persons with a heart rhythm disorder, cardiac scans required somewhat higher dosages (up to 4.1 mSv). Inter- and intra-observer variability was excellent (intra-class correlation coefficient was >0.99 for CAC).[19]

Participants were followed for a median of 5.0 years (interquartile range: 4.0 to 10.0 years). For this study, the final date of follow-up was January 2010. Information concerning the vital status of the participants was obtained from the municipal health service of Rotterdam. Participants in the Rotterdam Study were continuously monitored for the occurrence of cardiovascular events through automated linkage with the files from general practitioners in the research area of the Rotterdam Study. Information on study outcomes was gathered from general practitioners and from letters and discharge reports from medical specialists. Events were adjudicated by study physicians as described previously.[20] Incident CHD was defined as the occurrence of a definite non-fatal or fatal myocardial infarction, or death due to CHD.[20]Strokes were diagnosed when a patient had typical neurological symptoms and a computed tomography or magnetic resonance imaging, made within 4 weeks after the occurrence of stroke, confirmed the diagnosis.[21] The research physicians, cardiologist, and neurologist were not aware of participants' CAC score.

The Heinz Nixdorf Recall Study

The Heinz Nixdorf Recall Study is a population-based cohort study with subjects randomly selected from mandatory lists of residence. Study methods have been described in detail.[22-24] Briefly, 4,814 participants ages 45-75 years were recruited in the metropolitan Ruhr area in Germany and enrolled between 2000 and 2003. For the present analysis, we excluded those< 60 years of age; those with prior CHD, stroke, and HF at baseline; those who had any missing covariates; and those lost to follow-up. A total of 1,901 participants were included in this study. All participants gave their written informed consent, and the study was approved by the institutional local ethical committees.

During the baseline examination, computer-assisted interviews were conducted at the study center in Essen. The interviewers collected information about medical history, smoking status, and current use of medication. Current smoking was defined as a history of cigarette smoking during the past year. BP was measured seated with an automated

oscillometric BP device (Omron, HEM-705CP). The mean of the 2nd and 3rd BP of three measurements was used for the analysis. Standard enzymatic methods were used to measure total and HDL-C within 12 hours at one central laboratory.[22] Diabetes was defined as present in cases of physician-diagnosed diabetes, having a blood glucose of ≥200 mg/dL or fasting glucose of ≥126 mg/dL, or taking anti-diabetic medication.

Nonenhanced electron-beam CT scans were performed with a C-100 or C-150 scanner (GE Imatron, South San Francisco) at two sites in Bochum and Mülheim.[25] The scanners were operated in the single slice mode with an image acquisition time of 100ms and a section thickness of 3 mm. Prospective ECG-triggering was done at 80% of the R-R interval. Contiguous slices down to the apex of the heart were obtained. The CAC score was determined using the Agatston's method.[8] Coronary artery calcification was defined as at least four contiguous pixels with a CT density ≥130 Hounsfield Units. The total CAC score was computed, comprising all calcified lesions in the epicardial coronary system. Analyses were performed using a Virtuoso workstation (Siemens Medical Solutions, Forchheim, Germany).

Participants were followed for a median of 10.5 years (interquartile range: 9.5 to 12.2 years). For this study, the final date of follow-up was March 2015. For all primary study endpoints, hospital and nursing home records, including electrocardiograms, laboratory values, and pathology reports, were collected. For deceased subjects, death certificates were collected and interviews with general practitioners, relatives, and eyewitnesses were undertaken if possible. Medical records were obtained in 100% of all reported endpoints. An external endpoint committee blinded for risk factor status and CAC scores reviewed all documents and classified the endpoints. For the current analysis, CHD (myocardial infarction, sudden cardiac death, and CHD deaths) and stroke events were considered as the outcome. Myocardial infarction was defined based on symptoms, signs of electrocardiography, and enzymes (levels of creatine kinase), as well as troponin T or I, and necropsy as nonfatal acute myocardial infarction and coronary death.[26] Stroke event, defined as focal neurological deficits of presumed cerebrovascular origin that persisted over a period of ≥24 hours, were assessed in annual questionnaires and a follow-up visit. Stroke events were validated by an independent internal and external end point committee that provided consensus decisions in case of disagreements.[27]

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eTable 1. CT scan dates in each cohort

	CT scan dates	**Reporting of results**
Framingham Heart Study	2002-2005	Only CAC >90th percentile were reported to the participants and the physicians.
Multi-Ethnic Study of Atherosclerosis	2000-2002	Usually not reported to participants or physicians.
Cardiovascular Health Study	1998-2000	Results were sent to the physicians.
Rotterdam Study (RS)	RS-I:1997-2000 RS-II: 2003-2006	RS-I: Participants were not informed about the calcium score. RS-II: participants in the highest 10% of the CAC score distribution for men and the highest 5% for women were informed about their high calcium score and advised to visit their physicians.
Heinz Nixdorf Recall Study	2000-2003	Results were not sent to participants and physicians.

eTable 2. The frequency of ASCVD events and the corresponding incident rates (per 1,000 person-years) by race and CAC score in original cohorts

	Whites (n=2,347)		**African Americans (n=1,158)**		**Hispanic (n=810)**		**Asians (n=463)**	
	N (%)	CVD events, N (incident rates)	N (%)	CVD events. N (incident rates)	N (%)	CVD events, N (incident rates)	N (%)	CVD events, N (incident rates)
Agatston score=0,	540 (23)	26 (4.7; 3.2 to 7.0)	465 (40)	18 (3.9; 2.5 to 6.3)	306 (38)	18 (5.9; 3.7 to 9.3)	167 (36)	4 (2.3; 0.9 to 6.2)
Agatston score 1-100	659 (28)	76 (12.3; 9.8 to 15.4)	350 (30)	40 (11.8; 8.7 to 16.1)	274 (34)	29 (11.7; 8.2 to 16.9)	156 (34)	8 (5.3; 2.6 to 10.6)
Agatston score >100 and ≤300	452 (19)	78 (19.3; 15.5 to 24.1)	149 (13)	23 (17.6; 11.7 to 26.5)	104 (13)	21 (22.1; 14.4 to 33.8)	76 (16)	8 (11.4; 5.7 to 22.8)
Agatston score>300	696 (30)	168 (29.5; 25.4 to 34.4)	194 (17)	48 (31.0; 23.4 to 41.2)	126 (15)	24 (23.6; 15.8 to 35.2)	64 (14)	9 (15.5; 8.1 to 29.8)

The frequency of ASCVD events (N, %) and the corresponding incident rates (per 1,000 person-years) are presented.
ASCVD indicates atherosclerotic cardiovascular disease; CAC, coronary artery calcium; N, number; CVD, cardiovascular disease.

eTable 3. The frequency of cardiovascular outcomes and corresponding incidence rates (per 1,000 person-years) according to CAC categories in original cohorts (n=4778)

	ASCVD event, No. (per 1,000 person-years; 95% CIs)	**CHD event, No. (per 1,000 person-years; 95% CIs)**	**Stroke event, No. (per 1,000 person-years; 95% CIs)**
Overall (n=4,778)	598 (13.5; 12.5 to 14.7)	405 (9.0; 8.2 to 10.0)	228 (5.0; 4.4 to 5.7)
Agatston score=0 (n=1,478)	66 (4.5; 3.5 to 5.7)	33 (2.2; 1.6 to 3.1)	36 (2.4; 1.7 to 3.3)
Agatston score 1-100 (n=1,439)	153 (11.3; 9.6 to 13.2)	101 (7.4; 6.1 to 9.0)	57 (4.1; 3.2 to 5.4)
Agatston score >100 and ≤300 (n=781)	130 (18.6; 15.7 to 22.1)	87 (12.2; 9.9 to 15.1)	49 (6.8; 5.1 to 9.0)
Agatston score>300 (n=1,080)	249 (28.2; 24.9 to 31.9)	184 (20.2; 17.5-23.4)	86 (9.1; 7.4 to 11.2)

The incidence rates of cardiovascular outcomes by CAC categories are shown. ASCVD includes CHD and stroke. Each cardiovascular event rate differed by CAC categories (P<0.001). CAC indicates coronary artery calcium; ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; No, number; CI, confidence interval.

eTable 4. The frequency of cardiovascular outcomes and corresponding incident rates (per 1000 person-years) according to included cohorts

Outcomes	**MESA (n=3,876)**	**FHS (n=515)**	**CHS (n=387)**	**Rotterdam Study (n=3,089)**	**HNR (n=1,901)**
ASCVD event, No. (per 1,000 patient-years; 95% CIs)	380 (10.2; 9.3 to 11.3)	51 (14.3; 10.9 to 18.9)	167 (48.4; 41.6 to 56.3)	395 (18.8; 17.4, 20.2)	173 (9.0; 7.7 to 10.3)
CHD event, No. (per 1,000 patient-years; 95% CIs)	244 (6.5; 5.7 to 7.3)	32 (8.9; 6.3-12.5)	129 (36.5; 30.7 to 43.4)	229 (10.7; 9.3 to 12.1)	106 (5.3; 4.3 to 6.3)
Stroke event, No. (per 1,000 patient-years; 95% CIs)	154 (4.1; 3.5 to 4.8)	20 (5.4; 3.5-8.4)	54 (13.9; 10.7 to 18.2)	180 (7.9; 6.8 to 9.1)	77 (3.9; 3.0 to 4.7)

ASCVD includes CHD and stroke. ASCVD indicates atherosclerotic cardiovascular disease; CAC, coronary artery calcium; MESA, Multi-Ethnic Study of Atherosclerosis; FHS, Framingham Heart Study; CHS, Cardiovascular Health Study; HNR, Heinz Nixdorf Recall Study; No, number.

eTable 5. Discordance in predictive ability between age and CAC score in original cohort (n=4778)

		Model 2: 10-year ASCVD risk based upon CAC score			
		<5.0 %	**5.0 to <7.5%**	**≥7.5%**	
		Number (row %) ‹crude event rate %›			**Total**
Model 1: 10-year ASCVD risk based upon age	**<5.0 %**	533 (63.8) ‹1.7›	190 (22.7) ‹2.1›	113 (13.5) ‹8.8›	**836**
	5.0 to <7.5%	415 (42.1) ‹3.9›	201 (20.4) ‹4.5›	370 (37.5) ‹9.2›	**986**
	≥7.5%	298 (10.1) ‹3.7›	388 (13.1) ‹7.0›	2270 (76.8) ‹21.1›	**2,956**
	Total	**1,246**	**779**	**2,753**	**4,778**

Results are presented as n (row %) ‹crude event rate %›. We defined 3 groups: age > CAC score discordance (blue words), concordance (black words), and age < CAC score discordance (red words). For 10-year ASCVD risk prediction, Model 1 included age, sex, race (white, African American, Hispanic, and Asian), study sites (MESA, FHS, and CHS), current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs. Model 2 included log CAC (Agatston score +1), sex, race, study sites, current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs.

eTable 6. Model fit and HRs for incident cardiovascular outcomes in original cohorts (n=4778)

	ASCVD event (n=598)		CHD event (n=405)		Stroke event (n=228)	
Variable	**LR test**	**HRs (95% CIs) of CAC**	**LR test**	**HRs (95% CIs) of CAC**	**LR test**	**HRs (95% CIs) of CAC**
Model 1:						
Age, years	317.55	1.07 (1.06 to 1.09)‡	283.92	1.07 (1.05 to 1.09)‡	96.67	1.08 (1.06 to 1.11)‡
Model 2:						
CAC (1-100 vs. 0)	376.53	2.21 (1.65 to 2.95)‡	343.5	2.74 (1.84 to 4.07)‡	96.12	1.64 (1.07 to 2.50)*
CAC (>100 and ≤300 vs. 0)		3.64 (2.69 to 4.93)‡		4.47 (2.97 to 6.72)‡		2.77 (1.78 to 4.30)‡
CAC (>300 vs. 0)		4.84 (3.62 to 6.45)‡		6.22 (4.21 to 9.19)‡		3.50 (2.30 to 5.33)‡
Model 3:	385.61		351.40		100.57	
Log CAC (Agatston score +1)		1.26 (1.22 to 1.31)‡		1.82 (1.63 to 2.04)‡		1.22 (1.15 to 1.30)‡
Model 4:	420.54		370.81		121.34	
Age, years		1.05 (1.04 to 1.07)‡		1.05 (1.03 to 1.07)‡		1.06 (1.04 to 1.09)‡
CAC (1-100 vs. 0)		1.96 (1.46 to 2.63)‡		2.44 (1.64 to 3.64)‡		1.41 (0.92 to 2.16)
CAC (>100 and ≤300 vs. 0)		3.05 (2.25 to 4.15)‡		3.79 (2.51 to 5.72)‡		2.20 (1.40 to 3.45)†
CAC (>300 vs. 0)		3.84 (2.86 to 5.16)‡		5.00 (3.36 to 7.44)‡		2.62 (1.70 to 4.03)‡
Model 5:	426.78		376.28		124.19	
Age, years		1.05 (1.04 to 1.07)‡		1.05 (1.03 to 1.07)‡		1.06 (1.04 to 1.09)‡
Log CAC (Agatston score +1)		1.22 (1.17 to 1.27)‡		1.26 (1.20 to 1.52)‡		1.17 (1.10 to 1.25)‡

ASCVD included CHD and stroke. All models include sex, race, and study sites (MESA, FHS, and CHS). In Model 4 and Model 5, age and CAC score were analyzed jointly. CAC was used as a categorical variable (0, 1-100, 101-300, >300) and a continuous variable (Log [Agatston score +1]). LR test indicates Likelihood Ratio $\chi 2$; CAC, coronary artery calcium; ASCVD, ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; MESA, Multi-Ethnic Study of Atherosclerosis; FHS, Framingham Heart Study; CHS, Cardiovascular Health Study; HR, hazard ratio; CI, confidence interval. Statistical significance was defined as $P < 0.05$. *$P<0.05$; † $P<0.01$; ‡ $P<0.001$.

eTable 7. Predictive ability of CAC score alone versus age alone for cardiovascular outcomes in original cohorts (n=4778)

Variable	C-statistics (95% CI)	C statistics changes (95% CI)
ASCVD event (n=598)		
Model 1-1: Age, years	0.653 (0.621 to 0.685)	-
Model 1-2: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	0.688 (0.660 to 0.715)	Vs. model 1-1 0.035 (-0.005 to 0.074)
Model 1-3: Log CAC (Agatston score +1)	0.693 (0.665 to 0.721)	Vs. model 1-2 0.040 (-0.001to 0.080)
CHD event (n=405)		
Model 2-1: Age, years	0.658 (0.616 to 0.699)	-
Model 2-2: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	0.701 (0.669 to 0.733)	Vs. model 2-1 0.044 (-0.008 to 0.095)
Model 2-3: Log CAC (Agatston score +1)	0.708 (0.675 to 0.742)	Vs. model 2-1 0.051 (-0.001 to 0.103)
Stroke event (n=228)		
Model 3-1: Age, years	0.655 (0.608 to 0.702)	-
Model 3-2: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	0.662 (0.615 to 0.708)	Vs. model 3-1 0.007 (-0.051 to 0.065)
Model 3-3: Log CAC (Agatston score +1)	0.666 (0.620 to 0.713)	Vs. model 3-1 0.011 (-0.046 to 0.069)

ASCVD included CHD and stroke. Comparison of the discriminative ability between prediction models (reference: model including age alone) was conducted by Harrell's C statistics. Statistical significance was defined as P <0.05. *P<0.05.

eTable 8. Adding CAC score and removing age only from prediction models: model fit and HRs in original cohorts (n=4778)

Variable	Likelihood Ratio χ^2	HRs (95% CIs) of CAC
ASCVD event (n=598)		
Base model:	388.47	N/A
Model 1: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	432.0	2.10 (1.57-2.82)‡ 3.31 (2.44-4.49)‡ 4.21 (3.14-5.64)‡
Model 2: Log CAC (Agatston score +1)	439.98	1.24 (1.19-1.29)‡
CHD event (n=405)		
Base model:	314.04	N/A
Model 3: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	359.27	2.63 (1.77-3.91)‡ 4.15 (2.75-6.26)‡ 5.60 (3.77-8.31)‡
Model 4: Log CAC (Agatston score +1)	366.41	1.28 (1.22-1.34)‡
Stroke event (n=228)		
Base model:	158.20	N/A
Model 5: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	153.73	1.50 (0.98-2.29) 2.35 (1.50-3.67)‡ 2.75 (1.80-4.22)‡
Model 6: Log CAC (Agatston score +1)	157.56	1.18 (1.11-1.25)‡

ASCVD included CHD and stroke. The base model includes age, sex, race (white, African American, Hispanic, and Asian), study sites (MESA, FHS, and CHS), current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs. In Model 1-6, CAC score was added to models, with age only being removed. CAC was used as a categorical variable (0, 1-100, 101-300, >300) and a continuous variable (Log [Agatston score +1]). HRs associated with log CAC (Agatston score +1) represent each unit difference in the log-transformed calcium score.

ASCVD indicates atherosclerotic cardiovascular disease; CAC, coronary artery calcium; CHD, coronary heart disease; HF, heart failure; HR, hazard ratio; CI, confidence interval.

Statistical significance was defined as P <0.05. *P<0.05; † P<0.01; ‡ P<0.001.

eTable 9. Replacing CAC score for all risk factors but retaining age in prediction models: model fit, HRs, and C statistics in original cohorts (n=4778)

Variable	Likelihood Ratio $\chi 2$	HRs (95% CIs) of CAC	C-statistics (95% CI)	C statistics changes (95% CI) from base model
ASCVD event (n=598)				
Base model:	388.47	N/A	0.699 (0.669 to 0.728)	-
Model 1: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	420.54	1.96 (1.46-2.63)‡ 3.05 (2.25-4.15)‡ 3.84 (2.86-5.16)‡	0.721 (0.693 to 0.750)	0.022 (0.002 to 0.043)*
Model 2: Log CAC (Agatston score +1)	426.78	1.22 (1.17-1.27)‡	0.722 (0.693 to 0.751)	0.023 (0.003 to 0.044)*
CHD event (n=405)				
Base model:	314.04	N/A	0.703 (0.666 to 0.741)	-
Model 3: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	370.81	2.44 (1.64-3.64)‡ 3.79 (2.51-5.72)‡ 5.00 (3.36-7.44)‡	0.739 (0.705 to 0.773)	0.036 (0.011 to 0.060)†
Model 4: Log CAC (Agatston score +1)	376.28	1.26 (1.20-1.32)‡	0.740 (0.706 to 0.774)	0.037 (0.012 to 0.062)†
Stroke event (n=228)				
Base model:	158.20	N/A	0.717 (0.671 to 0.762)	-
Model 5: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	121.34	1.41 (0.92-2.16) 2.20 (1.40-3.45)† 2.62 (1.70-4.03)‡	0.694 (0.646 to 0.742)	-0.023 (-0.056 to 0.011)
Model 6: Log CAC (Agatston score +1)	124.19	1.17 (1.10-1.25)‡	0.699 (0.652 to 0.746)	-0.018(-0.051 to 0.153)

ASCVD included CHD and stroke. The base model includes age, sex, race (white, African American, Hispanic, and Asian), study sites (MESA, FHS, and CHS), current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, use of antihypertensive drugs and lipid-lowering drugs. In Model 1-6, CAC score was added to base models (including

age, sex, race, and study site), with risk factors (current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs) being removed.
Statistical significance was defined as $P < 0.05$. *$P<0.05$; † $P<0.01$; ‡ $P<0.001$.

eTable 10. Discordance in predictive ability between age and CAC score in the Rotterdam Study (n=3089)

		Model 2: 10-year ASCVD risk based upon CAC score			
		<5.0 %	**5.0 to <7.5%**	**≥7.5%**	
		Number (row %) ‹crude event rate %›			**Total**
Model 1: 10-year ASCVD risk based upon age	**<5.0 %**	8 (4.0) ‹0›	4 (0.9) ‹25.0›	7 (0.3) ‹0›	**19**
	5.0 to <7.5%	81 (40.3) ‹1.2›	52 (12.3) ‹0›	78 (3.2) ‹1.3›	**211**
	≥7.5%	112 (55.7) ‹5.3›	367 (86.8) ‹5.4›	2,380 (96.5) ‹16.9›	**2,859**
	Total	**201**	**423**	**2,465**	**3,089**

Results are presented as n (row %) ‹crude event rate %›. We defined 3 groups: age > CAC score discordance (blue words), concordance (black words), and age < CAC score discordance (red words). For 10-year ASCVD risk prediction, Model 1 included age, sex, current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs. Model 2 included log CAC (Agatston score +1), sex, current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs.

eTable 11. Discordance in predictive ability between age and CAC score in the Heinz Nixdorf Recall (n=1901)

		Model 2: 10-year ASCVD risk based upon CAC score			
		<5.0 %	**5.0 to <7.5%**	**≥7.5%**	
		Number (row %) ‹crude event rate %›			**Total**
Model 1: 10-year ASCVD risk based upon age	**<5.0 %**	500 (66.5) ‹2.2›	96 (12.8) ‹6.3›	156 (20.7) ‹6.4›	**752**
	5.0 to <7.5%	94 (32.9) ‹5.3›	73 (25.5) ‹8.2›	119 (41.6) ‹8.4›	**286**
	≥7.5%	74 (8.6) ‹10.8›	132 (15.3) ‹7.6›	657 (76.1) ‹16.3›	**863**
	Total	**668**	**301**	**932**	**1,901**

Results are presented as n (row %). We defined 3 groups: age > CAC score discordance (blue words), concordance (black words), and age < CAC score discordance (red words). For 10-year ASCVD risk prediction, Model 1 included age, sex, current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs. Model 2 included log CAC (Agatston score +1), sex, current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs.

eTable 12. Replacing CAC score for all risk factors but retaining age in prediction models: C statistics in confirmation cohorts (n=4990)

	The Rotterdam Study (n=3,089)		The Heinz Nixdorf Recall Study (n=1,901)	
Variable	**C-statistics (95% CI)**	**C statistics changes (95% CI) from base model**	**C-statistics (95% CI)**	**C statistics changes (95% CI) from base model**
ASCVD event (n=395)			**ASCVD events (n=173)**	
Base model:	0.657 (0.628 to 0.686)	-	0.682 (0.625 to 0.739)	-
Model 1: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	0.681 (0.652 to 0.711)	0.024 (-0.003 to 0.051)	0.721 (0.671 to 0.771)	0.039 (-0.08 to 0.086)
Model 2: Log CAC (Agatston score +1)	0.689 (0.664 to 0.714)	0.032 (0.010 to 0.054)	0.739 (0.690 to 0.787	0.057 (0.078 to 0.106)
CHD event (n=229)			**CHD event (n=106)**	
Base model:	0.666 (0.626 to 0.706)	-	0.677 (0.596 to 0.758)	-
Model 3: CAC (1-100 vs. 0) CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)	0.700 (0.663 to 0.738)	0.034 (-0.005 to 0.100)	0.741 (0.672 to 0.811)	0.064 (-0.009 to 0.137)
Model 4: Log CAC (Agatston score +1)	0.709 (0.675 to 0.744)	0.043 (0.001 to 0.096)	0.775 (0.717 to 0.832)	0.098 (0.027 to 0.168)
Stroke event (n=180)			**Stroke events (n=77)**	
Base model:	0.699 (0.653 to 0.744)	-	0.719 (0.643 to 0.795)	-
Model 5: CAC (1-100 vs. 0)	0.685 (0.640 to 0.731)	-0.013 (-0.038 to .011)	0.714 (0.635;0.794)	-0.005 (-0.060 to 0.051)

CAC (>100 and ≤300 vs. 0) CAC (>300 vs. 0)				
Model 6: Log CAC (Agatston score +1)	0.691 (0.647 to 0.736)	-0.007 (-0.052 to 0.038)	0.731 (0.657 to 0.806)	0.012 (-0.040 to 0.065)

ASCVD included CHD and stroke. The base model includes age, sex, current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs. In Model 1-6, CAC score was added to base models (including age, sex, race, and study site), with risk factors (current smoking, SBP, total cholesterol, HDL cholesterol, diabetes, use of antihypertensive drugs and lipid-lowering drugs) being removed.

eTable 13. Change in ASCVD risk stratification by CAC score and age in the Rotterdam Study (n=3,089)

Model 1: ASCVD risk stratification by CAC score					
Base model (predicted risk)	**Base model + Log CAC (predicted risk)**			**Category-based NRI (SE)**	**Category-free NRI (95% CIs)**
	<7.5%	≥7.5%	Total		
Participants who experienced ASCVD events					
<7.5%	1	1	2	-0.060 (-0.087 to -0.047)	0.452 (0.362 to 0.54)
≥7.5%	27	403	430		
Total	28	404	432		
Participants who did not experience ASCVD events					
<7.5%	25	17	42	0.208 (0.170 to 0.278)	
≥7.5	571	2,044	2,615		
Total	596	2,061	2,657		
Model 2: ASCVD risk stratification by age					
Base model (predicted risk)	**Base model + age (predicted risk)**			**Category-based NRI (SE)**	**Category-free NRI (95% CIs)**
	<7.5%	≥7.5%	Total		
Participants who experienced ASCVD events					
<7.5%	0	2	2	-0.002 (-0.023 to 0.013)	0.310 (0.209 to 0.411)
≥7.5%	3	427	430		
Total	3	429	432		
Participants who did not experience ASCVD events					
<7.5%	30	12	42	0.069 (0.051 to 0.102)	
≥7.5	197	2,418	2,615		
Total	227	2,430	2,657		

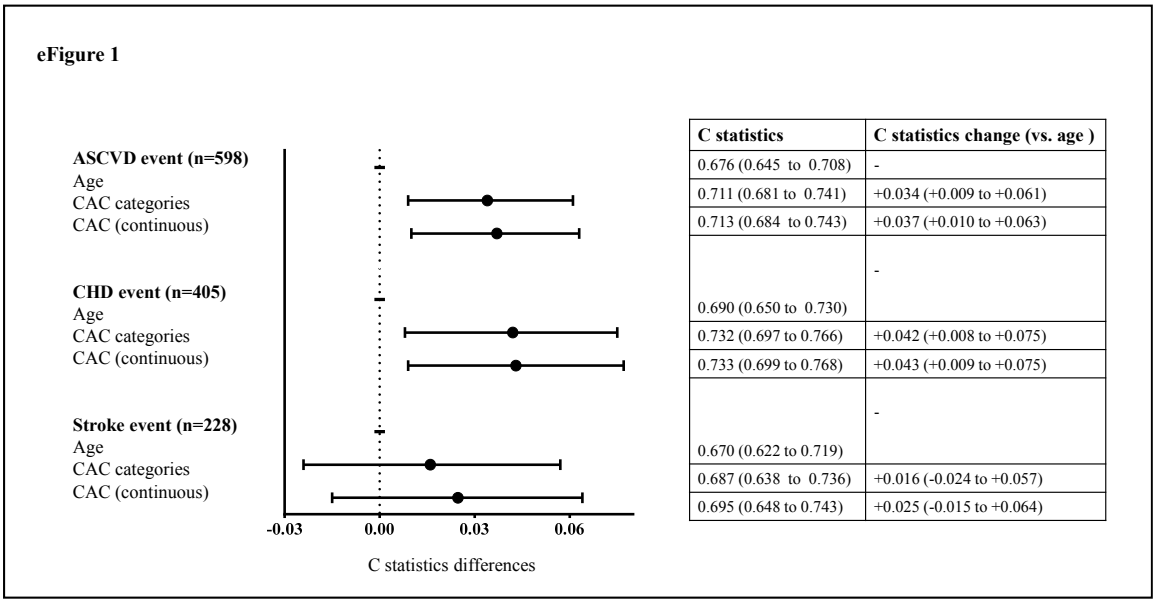
Reclassification tables are separated for cases and non-cases with rows indicating the risk categories based on the base model and columns indicating the new risk stratification after the addition of Log CAC (Agatston score +1) (Model 1) or age (Model 2) to the base model. The base model included sex, current smoking, systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs. The cells note the number of participants reclassified by predicted risk. **P*<0.05. NRI indicates net reclassification improvement.

eTable 14. Change in ASCVD risk stratification by CAC score and age in the Heinz Nixdorf Recall (n=1,901)

Model 1: ASCVD risk stratification by CAC score					
Base model (predicted risk)	**Base model + Log CAC (predicted risk)**			**Category-based NRI (SE)**	**Category-free NRI (95% CIs)**
	<7.5%	≥7.5%	Total		
Participants who experienced ASCVD events					
<7.5%	29	20	49	0.026 (-0.050 to 0.101)	0.291 (0.141 to 0.471)
≥7.5%	19	105	124		
Total	48	125	173		
Participants who did not experience ASCVD events					
<7.5%	789	160	949	0.026 (0.003 to 0.048)	0.144 (0.095 to 0.192)
≥7.5	201	578	779		
Total	990	738	1,728		
Model 2: ASCVD risk stratification by age					
Base model (predicted risk)	**Base model + age (predicted risk)**			**Category-based NRI (SE)**	**Category-free NRI (95% CIs)**
	<7.5%	≥7.5%	Total		
Participants who experienced ASCVD events					
<7.5%	36	13	49	-0.006 (-0.073 to 0.055)	0.094 (-0.073 to 0.256)
≥7.5%	14	110	124		
Total	50	123	173		
Participants who did not experience ASCVD events					
<7.5%	832	117	949	0.036 (0.011 to 0.053)	0.196 (0.154 to 0.252)
≥7.5	180	599	779		
Total	1,012	716	1,728		

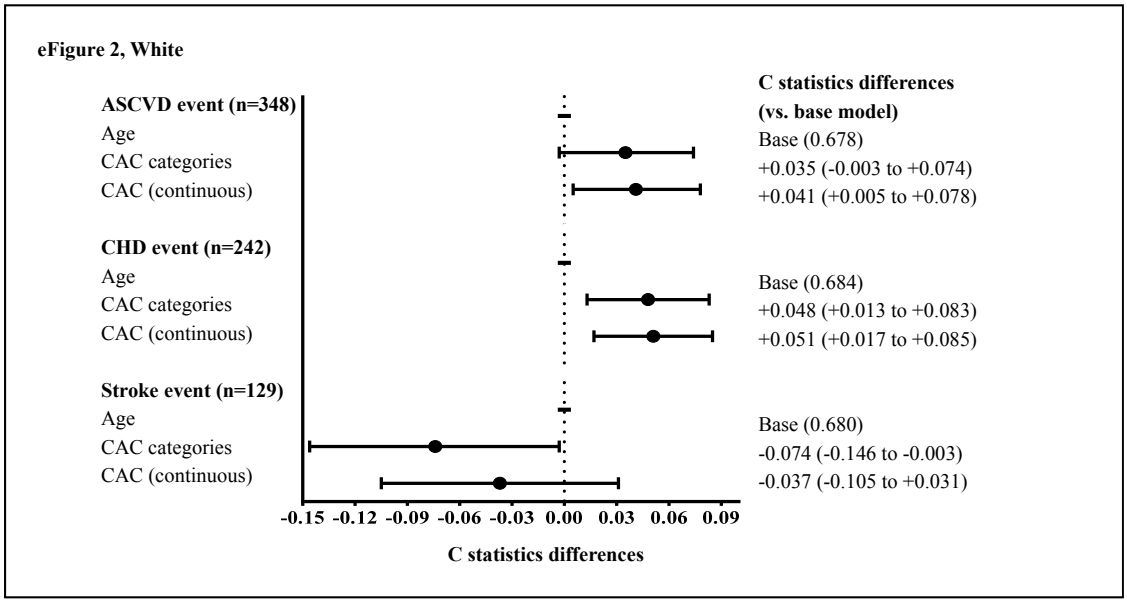
Reclassification tables are separated for cases and non-cases with rows indicating the risk categories based on the base model and columns indicating the new risk stratification after the addition of Log CAC (Agatston score +1) (Model 1) or age (Model 2) to the base model. The base model included sex, current smoking, systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs. The cells note the number of participants reclassified by predicted risk. **P*<0.05. NRI indicates net reclassification improvement.

eFigure 1. Predictive ability of CAC score versus age for cardiovascular outcomes

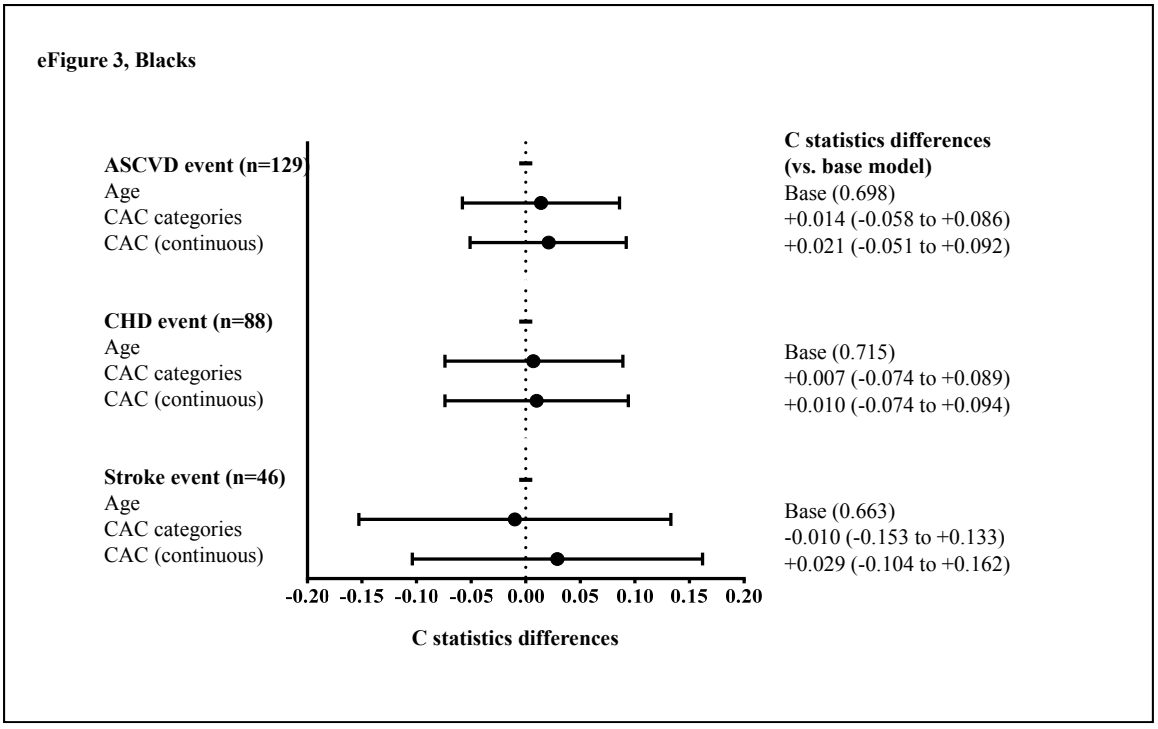


C statistics	C statistics change (vs. age)
0.676 (0.645 to 0.708)	-
0.711 (0.681 to 0.741)	+0.034 (+0.009 to +0.061)
0.713 (0.684 to 0.743)	+0.037 (+0.010 to +0.063)
0.690 (0.650 to 0.730)	-
0.732 (0.697 to 0.766)	+0.042 (+0.008 to +0.075)
0.733 (0.699 to 0.768)	+0.043 (+0.009 to +0.075)
0.670 (0.622 to 0.719)	-
0.687 (0.638 to 0.736)	+0.016 (-0.024 to +0.057)
0.695 (0.648 to 0.743)	+0.025 (-0.015 to +0.064)

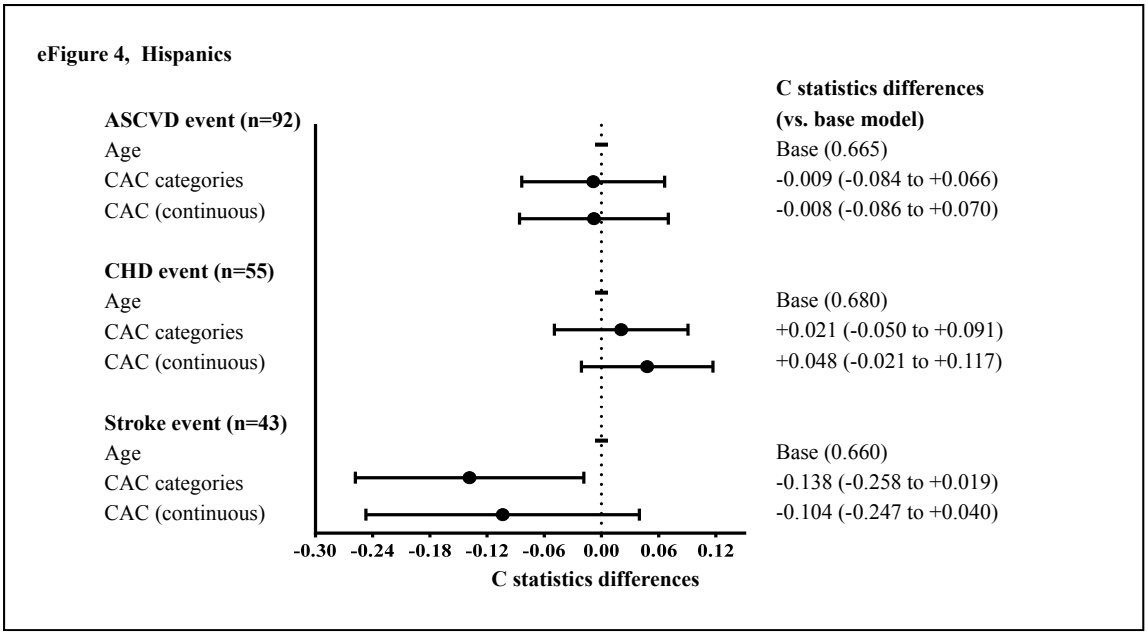
eFigure 2. Race-specific predictive ability of CAC score versus age for cardiovascular outcomes



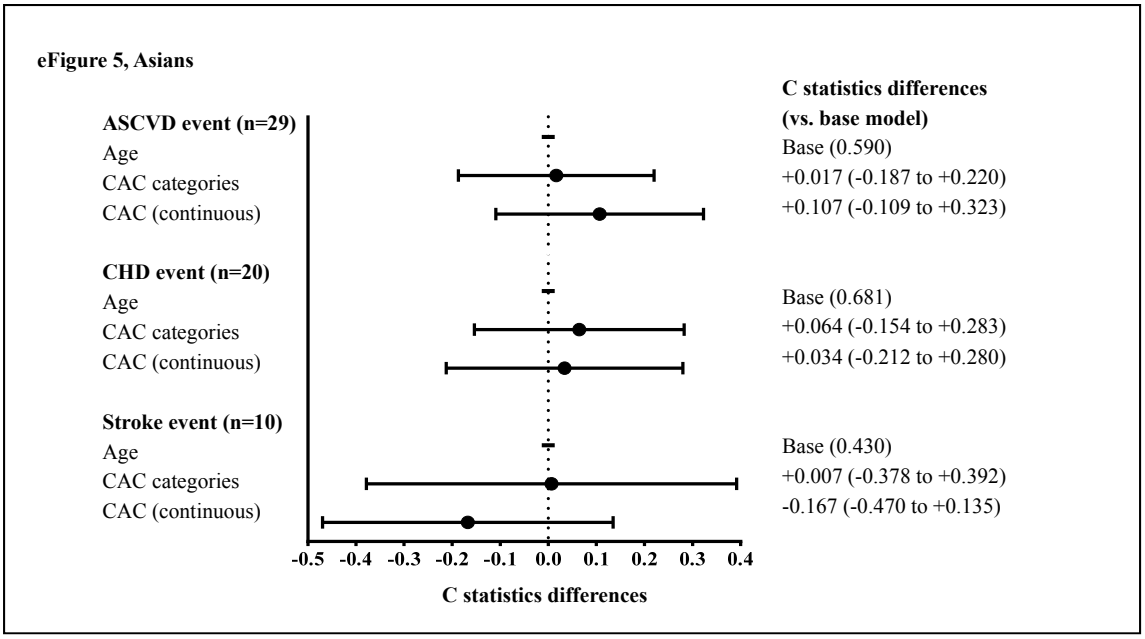
eFigure 3. Race-specific predictive ability of CAC score versus age for cardiovascular outcomes



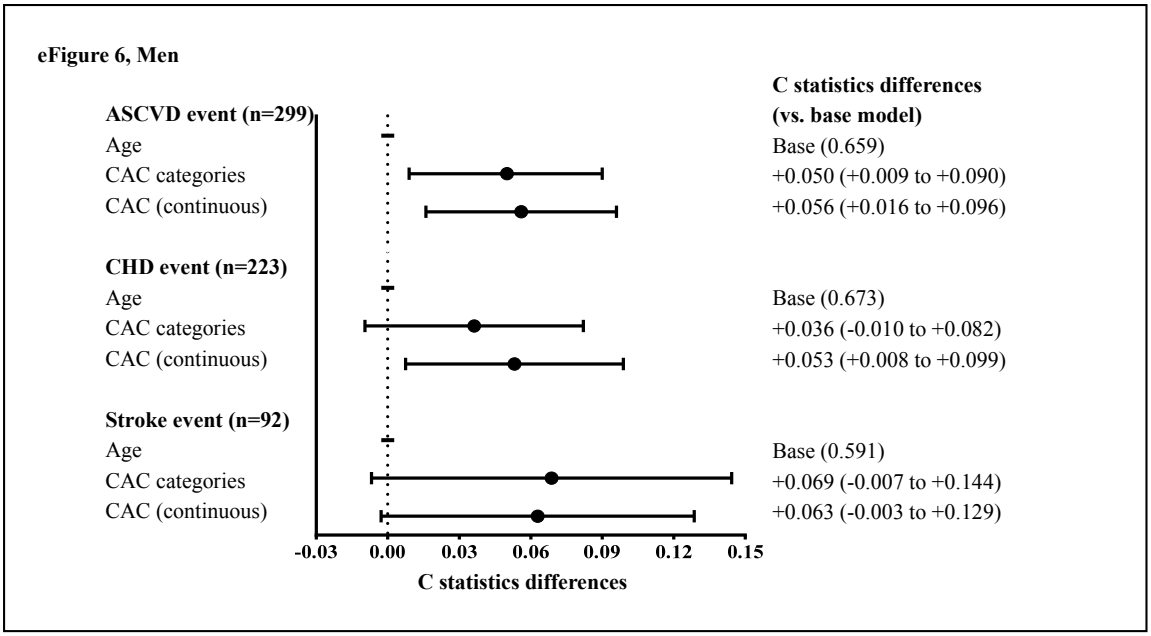
eFigure 4. Race-specific predictive ability of CAC score versus age for cardiovascular outcomes



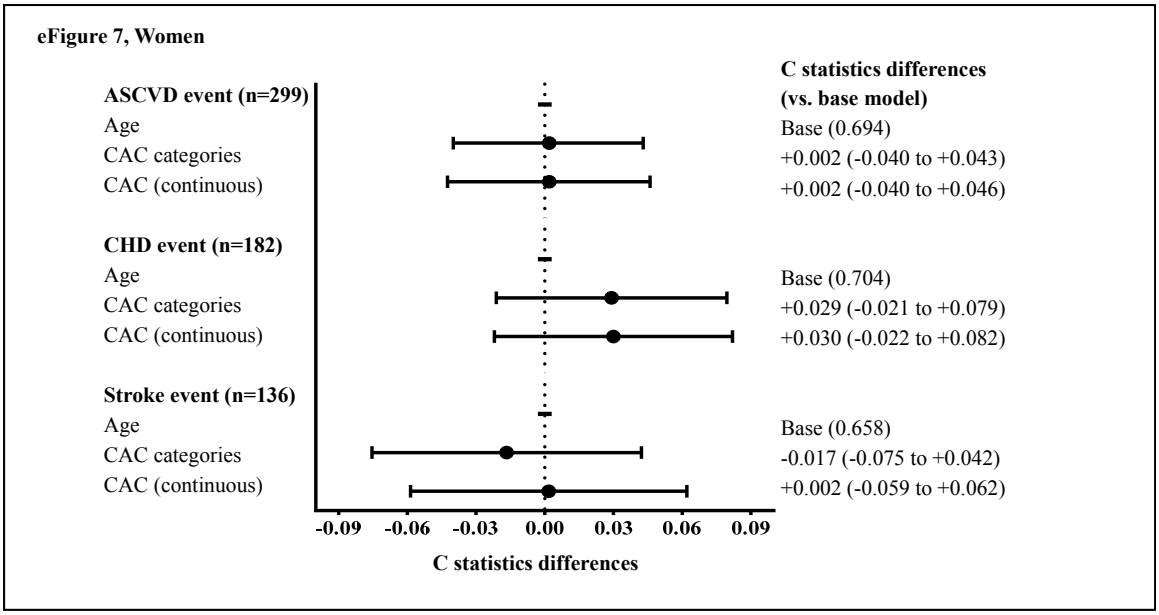
eFigure 5. Race-specific predictive ability of CAC score versus age for cardiovascular outcomes



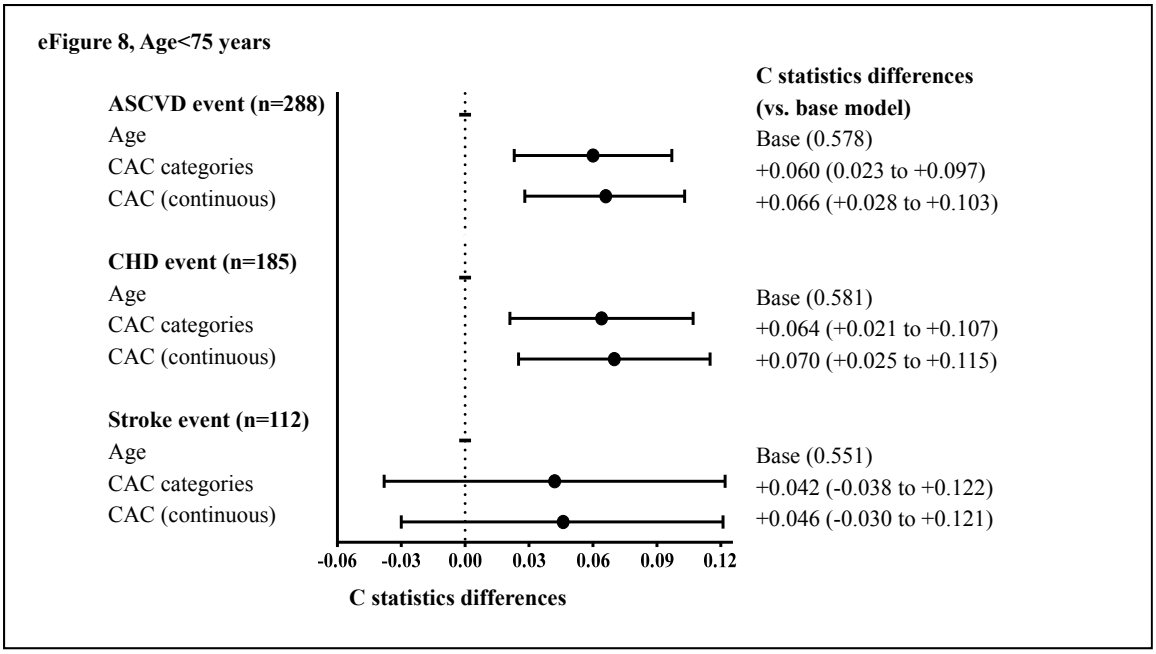
eFigure 6. Sex-specific predictive ability of CAC score versus age for cardiovascular outcomes



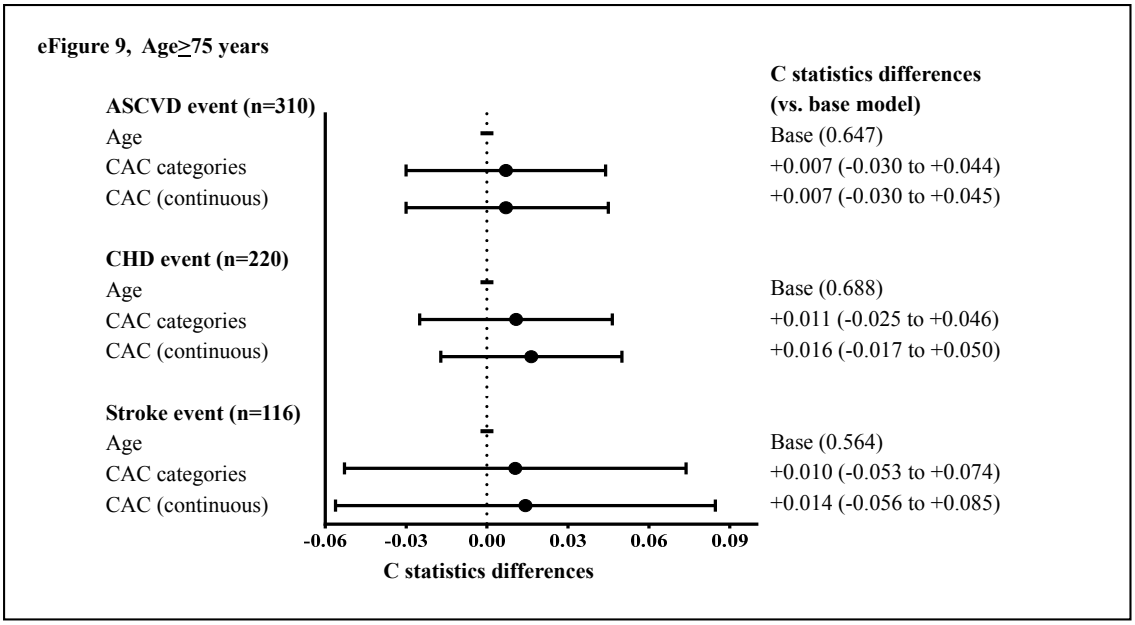
eFigure 7. Sex-specific predictive ability of CAC score versus age for cardiovascular outcomes



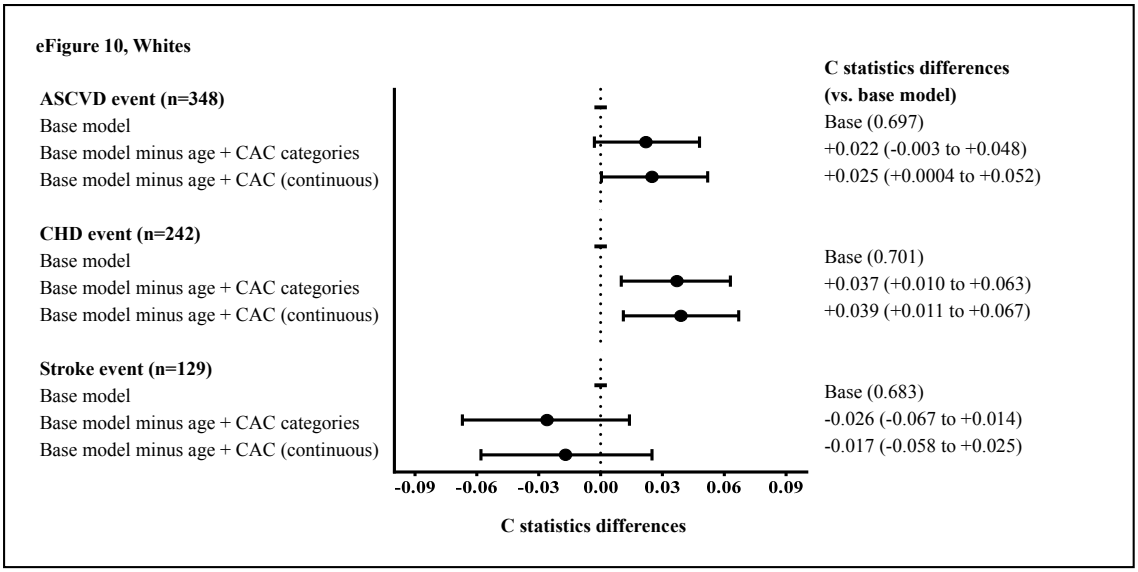
eFigure 8. Age-specific (<75 years and >75 years) predictive ability of CAC score versus age for cardiovascular outcomes



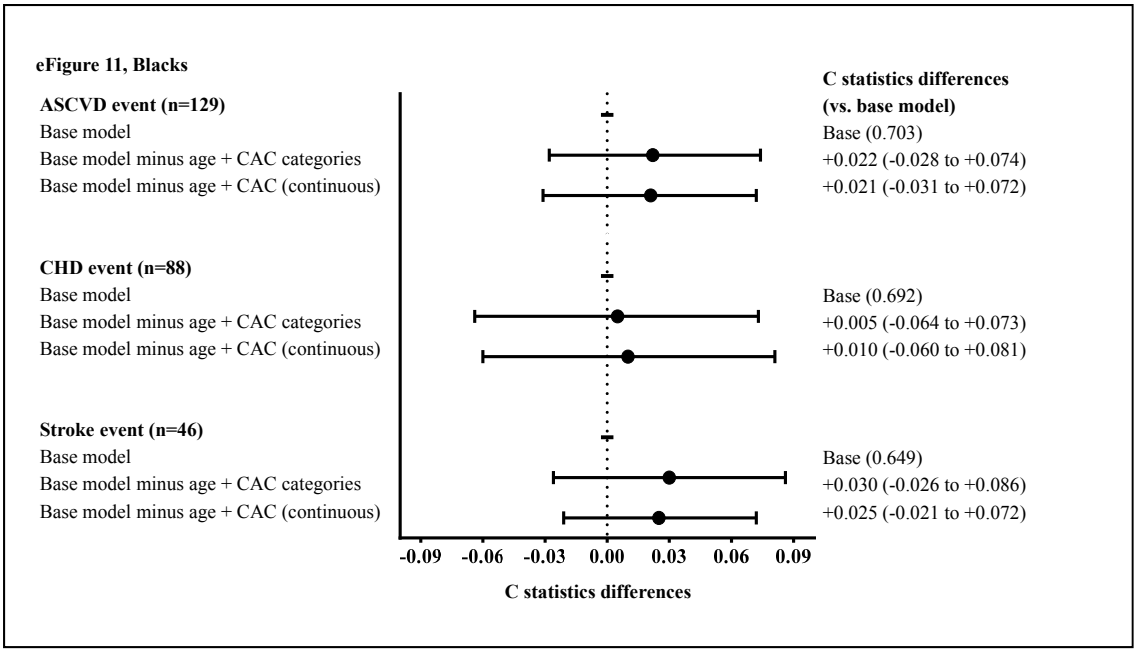
eFigure 9. Age-specific (<75 years and >75 years) predictive ability of CAC score versus age for cardiovascular outcomes



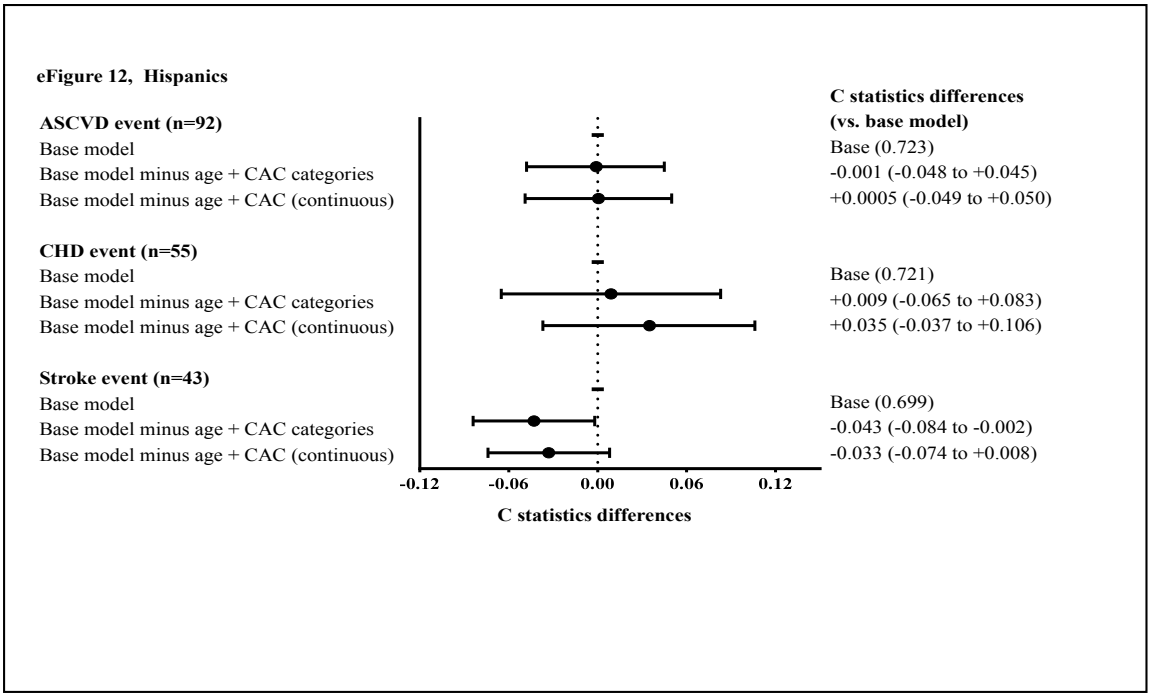
eFigure 10. Race-specific predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes



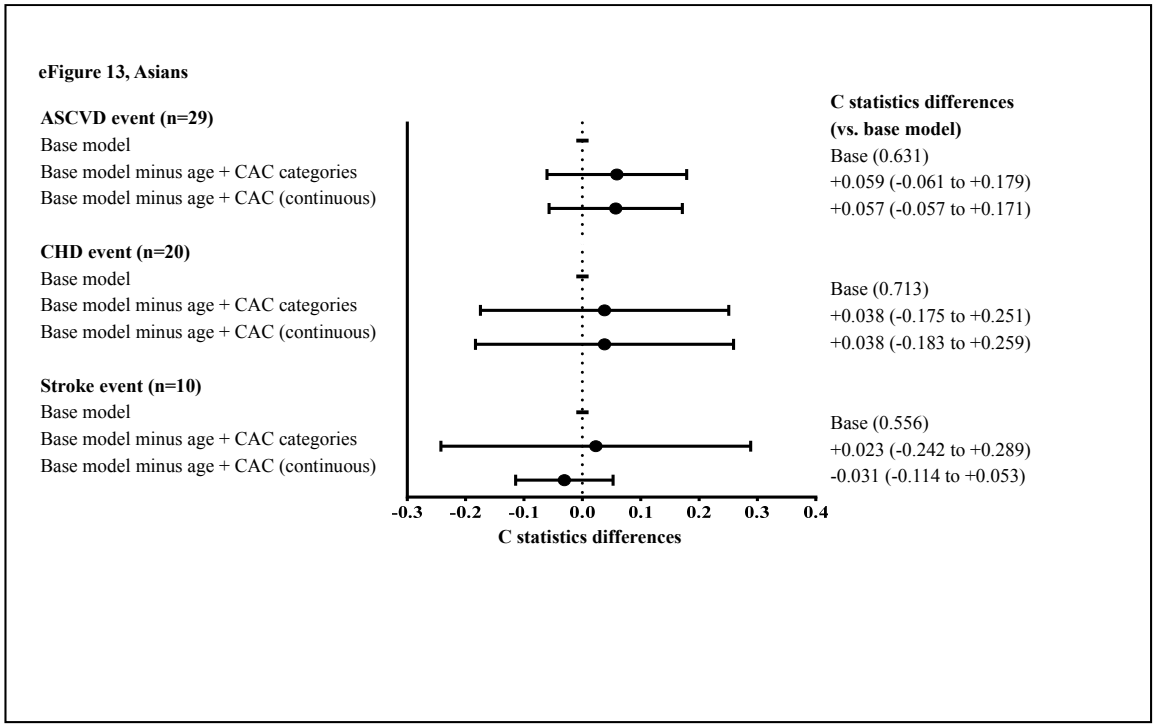
eFigure 11. Race-specific predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes



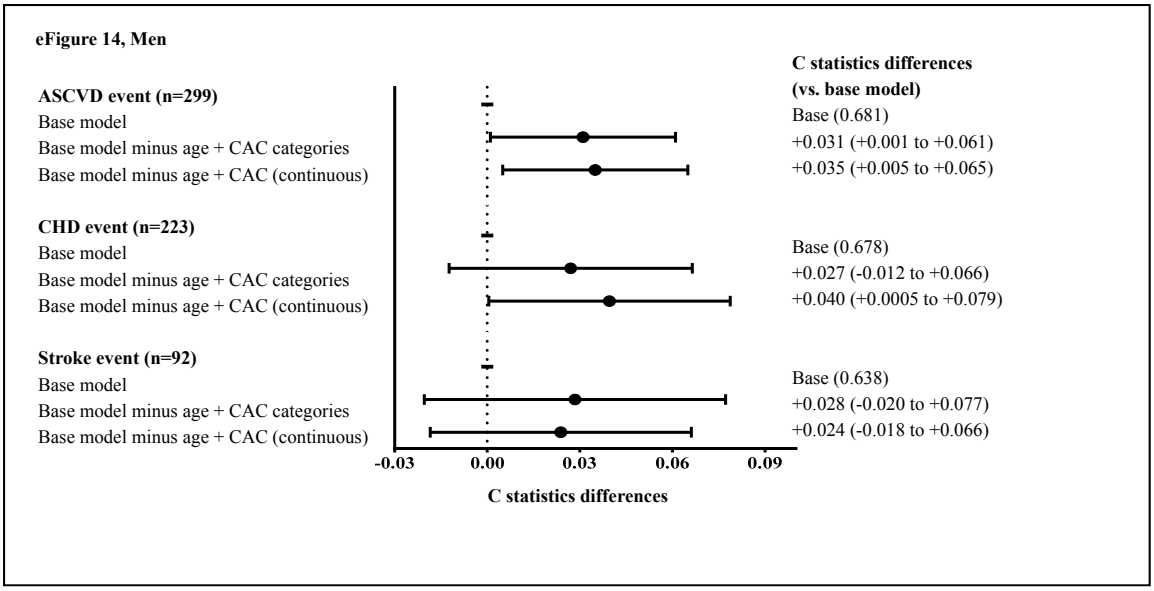
eFigure 12. Race-specific predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes



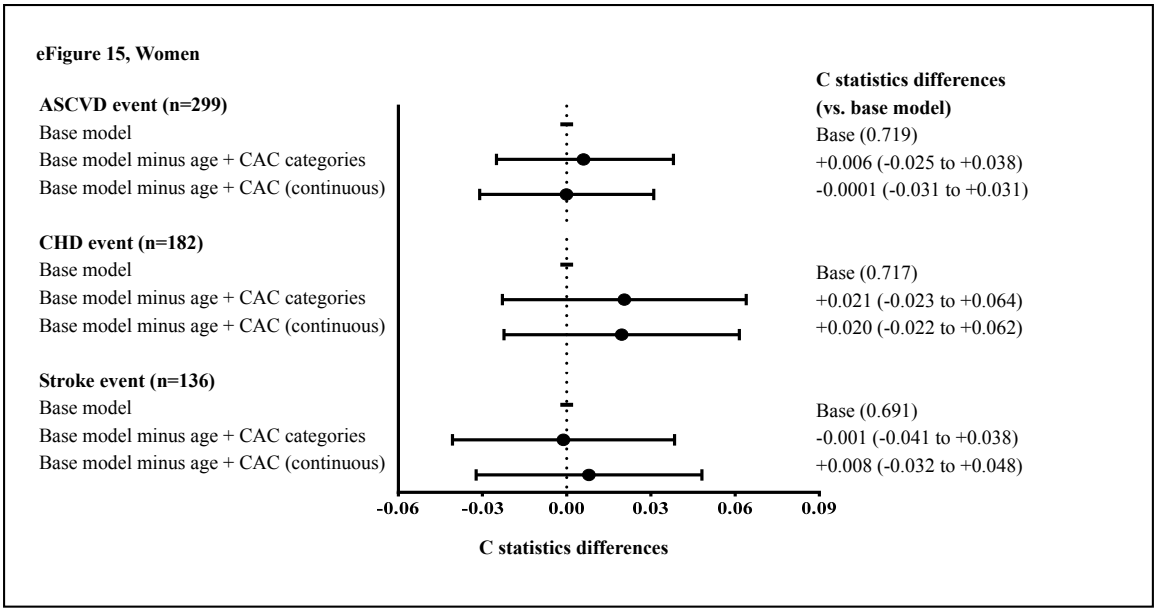
eFigure 13. Race-specific predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes



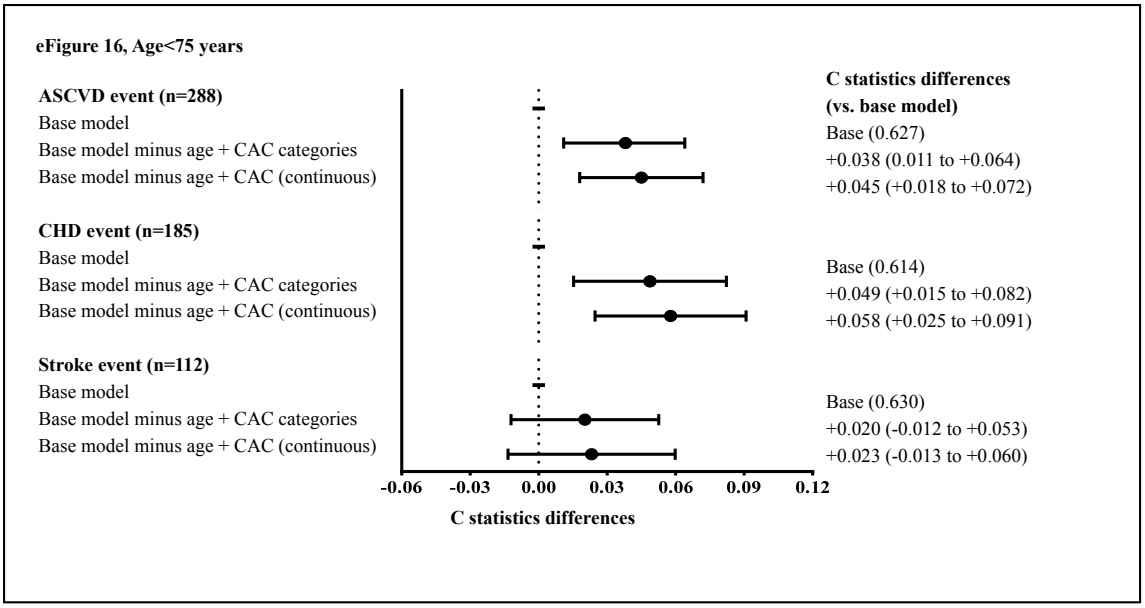
eFigure 14. Sex-specific predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes



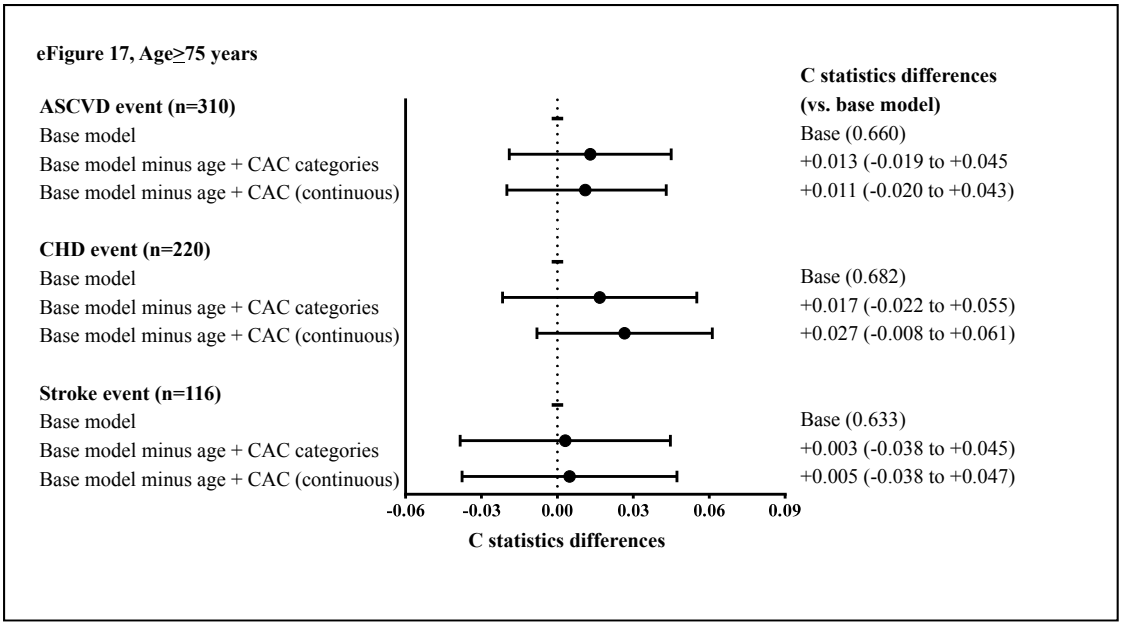
eFigure 15. Sex-specific predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes



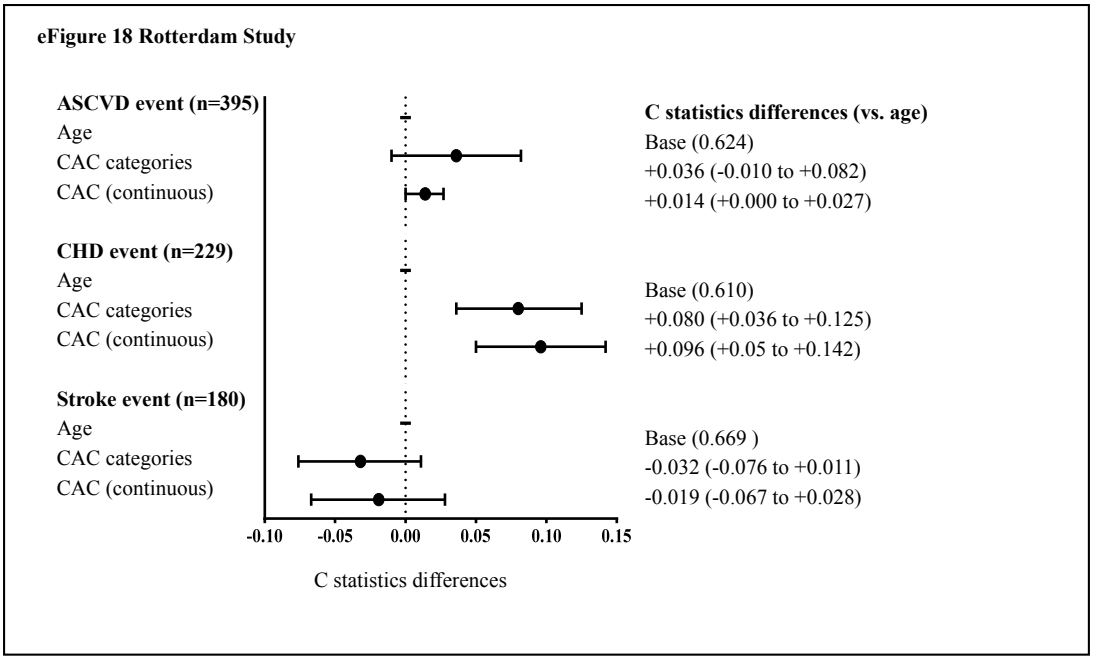
eFigure 16. Age-specific (<75 years and >75 years) predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes



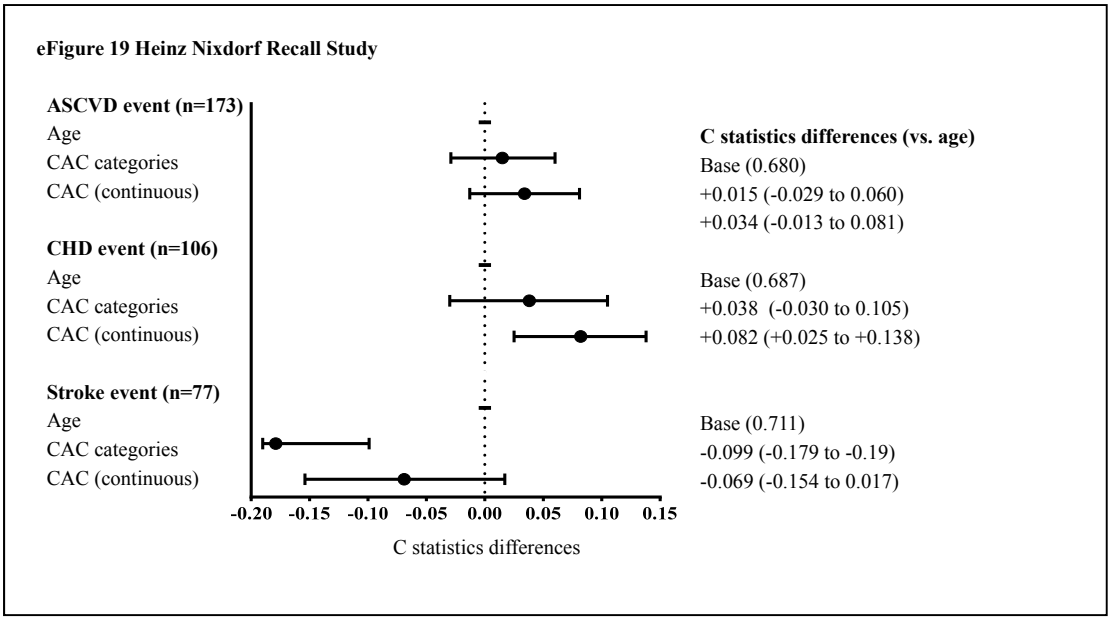
eFigure 17. Age-specific (<75 years and >75 years) predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes



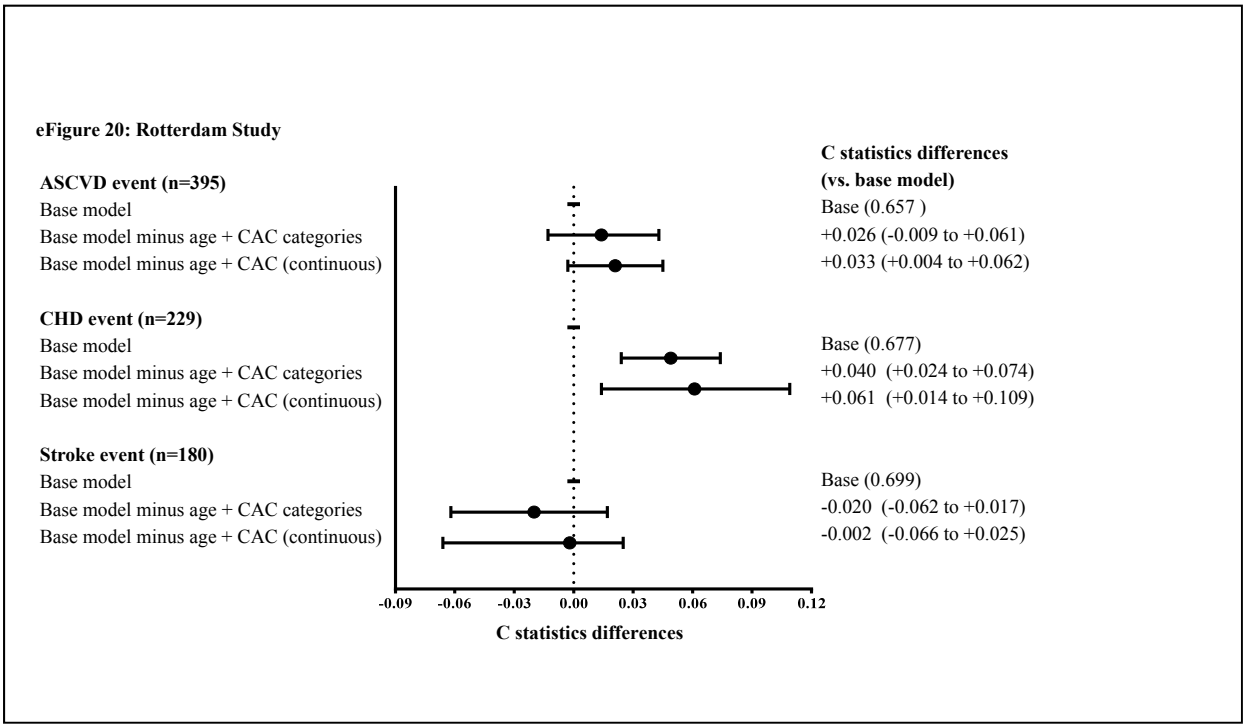
eFigure 18. Predictive ability of CAC score versus age for cardiovascular outcomes; external confirmation by the Rotterdam Study and the Heinz Nixdorf Recall Study



eFigure 19. Predictive ability of CAC score versus age for cardiovascular outcomes; external confirmation by the Rotterdam Study and the Heinz Nixdorf Recall Study



eFigure 20. Predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes; external confirmation by the Rotterdam Study and the Heinz Nixdorf Recall Study



eFigure 21. Predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes; external confirmation by the Rotterdam Study and the Heinz Nixdorf Recall Study

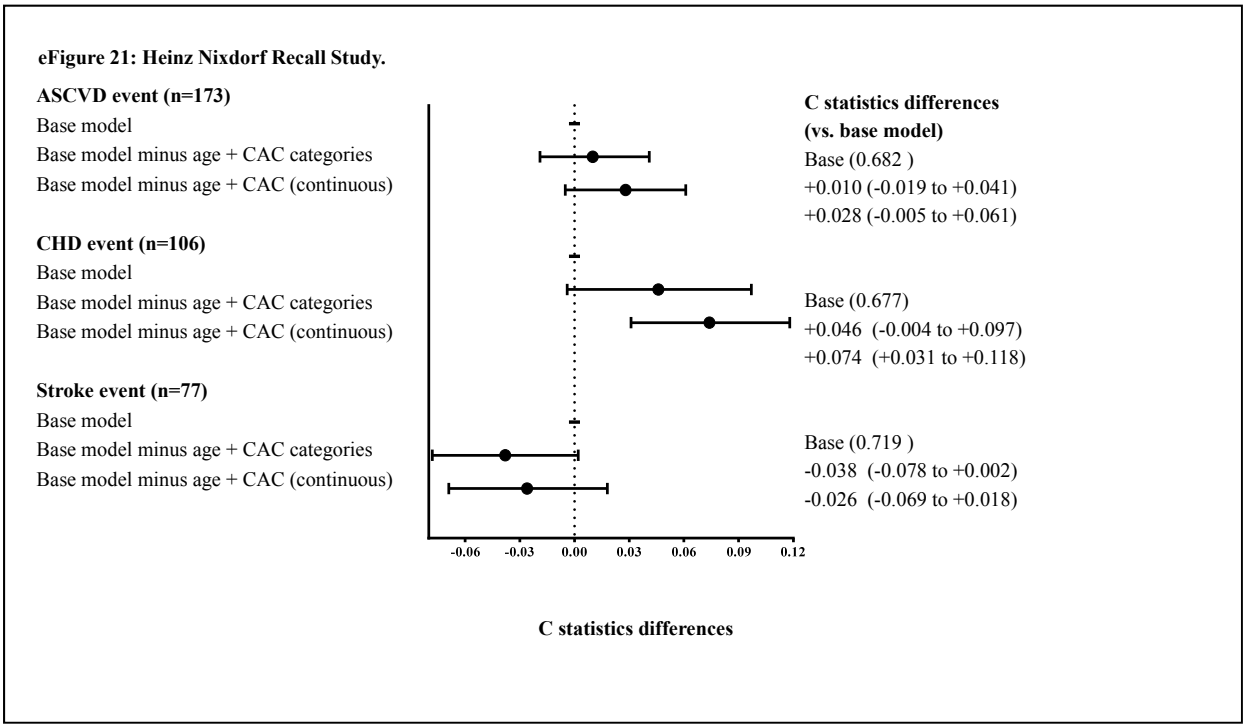


Figure Legends

eFigure 1
Predictive ability of CAC score versus age for cardiovascular outcomes
Figure shows differences in C statistics and 95% CIs for individual cardiovascular outcome between CAC score and age. All models includes sex, race, and study site. CAC score was tested as a categorical variable (0, 1 to 100, 101 to 300, and >300) and as a continuous variable (log [Agatston score+1] transformation).

eFigure 2-9
Predictive ability of CAC score versus age for cardiovascular outcomes; race-, sex-, and age (<75 years and ≥75years)-specific analysis
Figure shows difference in C statistics and 95% CIs for individual cardiovascular outcome between CAC score and age. All models includes sex, race, and study site. CAC score was tested as a categorical variable (0, 1 to 100, 101 to 300, and >300) and as a continuous variable (log [Agatston score +1] transformation).

CAC indicates coronary artery calcium; ASCVD, cardiovascular disease; CHD, coronary heart disease.

eFigure 10-17
Predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes; race-, sex-, and age (<75 years and ≥75years)-specific analysis
Figure shows difference in C statistics and 95% CIs for individual cardiovascular outcome after CAC score was added to base models including covariates, with age only being removed.
The base model includes age and the following covariates: sex, race, study site, current smoking, systolic blood pressure, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs. CAC score was tested as a categorical variable (0, 1 to 100, 101 to 300, and >300) and as a continuous variable (log [Agatston score +1] transformation).

eFigure 18-19
Predictive ability of CAC score versus age for cardiovascular outcomes; external confirmation by the Rotterdam Study and the Heinz Nixdorf Recall Study.
Figure shows difference in C statistics and 95% CIs for individual cardiovascular outcome between CAC score and age. All models includes sex. CAC score was tested as a categorical variable (0, 1 to 100, 101 to 300, and >300) and as a continuous variable (log [Agatston score +1] transformation).

eFigure 20-21
Predictive ability of risk factor covariates with CAC score and without age for cardiovascular outcomes; external confirmation by the Rotterdam Study and the Heinz Nixdorf Recall Study.

Figure shows difference in C statistics and 95% CIs for individual cardiovascular outcome after CAC score was added to base models including covariates, with age only being removed.
The base model includes age and the following covariates: sex, current smoking, systolic blood pressure, total cholesterol, HDL cholesterol, diabetes, and use of antihypertensive drugs and lipid-lowering drugs. CAC score was tested as a categorical variable (0, 1 to 100, 101 to 300, and >300) and as a continuous variable (log [Agatston score +1] transformation).