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ORIGINAL RESEARCH

Derivation of a Coronary Age Calculator Using Traditional Risk Factors and Coronary Artery Calcium: The Multi-Ethnic Study of Atherosclerosis

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BACKGROUND: The optimal method for communicating coronary heart disease (CHD) risk to individual patients is not yet clear. Recent research supports the concept of "coronary age" for more effective risk communication. We defined an individual's coronary age as the age at which an average healthy individual would have an equivalent estimated CHD risk as that calculated for the index individual, building on our previously validated MESA (Multi-Ethnic Study of Atherosclerosis) 10-year CHD Risk Score equations with and without coronary artery calcium (CAC).

METHODS AND RESULTS: We derived a coronary age by (1) calculating the MESA 10-year CHD risk; (2) mathematically setting this equal to an equation describing risk of an average healthy MESA participant, as a function of age; and (3) solving for age. The risk discrimination of the resultant coronary age was compared with that of chronological age, the MESA CHD Risk Score, and CAC alone. Approximately 95% of coronary age values ranged from 30 years less to 30 years higher than chronological age. Although the mean chronological age of individuals experiencing CHD events compared with those free of events was 67.4 versus 61.8 years, the difference in coronary age including CAC was larger (80.6 versus 62.8 years). Coronary age with CAC had identical predictive ability to that of MESA CHD Risk Score and outperformed chronological age and CAC alone.

CONCLUSIONS: The newly derived coronary age is a convenient transformation of MESA CHD Risk, retaining very good risk discrimination. This easy-to-communicate tool will be available for patients and clinicians, potentially facilitating risk communication in routine care.

Key Words: atherosclerosis ■ cardiovascular disease ■ coronary age ■ coronary artery calcium ■ risk communication ■ risk prediction

The global burden of cardiovascular disease (CVD) is high and still rising, resulting in CVD being the leading cause of death globally.[1–5] Accurate risk prediction remains the cornerstone of decision-making in the primary prevention of CVD,[6,7] although ease of communication and understanding of predicted risk remain equally as important. Despite this, the optimal method for communicating risk to individual patients is not clear. The traditional method of expressing CVD risk as a probability of an event over the subsequent 10 years has important shortcomings. For example, poor understanding of this metric by patients[8,9] may lead to inaccurate perception of susceptibility to CVD. This may impair patient motivation and ultimately inhibit the effectiveness of preventive care.[10–12]

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CLINICAL PERSPECTIVE

What Is New?

- Coronary age represents a convenient transformation of the MESA (Multi-Ethnic Study of Atherosclerosis) Coronary Heart Disease Risk Score into a familiar age scale.

What Are the Clinical Implications?

- Potentially improved ease of communication may enable coronary age to facilitate risk communication in preventive care.
- The performance of the new coronary age tool against the current standard risk scores needs further investigation, and the effect on everyday risk communication requires validation.

Nonstandard Abbreviations and Acronyms

MESA	Multi-Ethnic Study of Atherosclerosis
SBP	systolic blood pressure

The concept of "risk age" has been proposed to facilitate risk communication to patients.[13–17] Using this approach, which contrasts a patient's chronological age with their vascular age, patients are given a biological age equivalent to their estimated risk. For example, a 55-year-old man with several cardiovascular risk factors could be told that his coronary arteries are "as old as a those of a 70-year-old (healthy) man." It has been proposed that this approach to risk communication may increase patient understanding of risk estimations and, therefore, adherence to recommended lifestyle changes and pharmacotherapies.

Previous methods of estimating risk age have had, however, some shortcomings that limit their utility in current clinical practice. For instance, the "heart age" derived from the Framingham Study retains the problem of overestimation of CVD risk, which has been observed when using the Framingham Risk Score in contemporary populations.[14,18] The "arterial age" method developed by McClelland et al in the MESA (Multi-Ethnic Study of Atherosclerosis) study used onlycoronary artery calcium (CAC) information and therefore did not capture prognostic information from other important factors in estimating CHD risk.[13]

In this study we aimed to derive a "coronary age" calculator using the MESA 10-year coronary heart disease (CHD) Risk Score equations with and without the addition of CAC information. We then evaluated the predictive ability of this simple measure for CHD risk prediction as compared with other tools such as the CAC score, chronological age, and the MESA CHD risk score. A mobile application has also been developed to facilitate the use of coronary age for risk communication purposes in clinical practice.

METHODS

Data Sharing

Qualified researchers may request source data from MESA (https://www.mesa-nhlbi.org) and details about the specific may request the study protocol from Amgen, subject to an approved data sharing agreement clinical studies (http://www.amgen.com/datasharing).

Study Design

MESA is a US-based, observational, prospective cohort study that was initiated in 2000 aimed at determining the age, sex, and racial/ethnic differences in the prevalence, risk factors, and the progression of subclinical CVD. A detailed description of the design and methods of MESA has been previously published.[19] Briefly, from 6 US field centers (Forsyth County, NC; Bronx and Northern Manhattan, NY; Baltimore City and County, MD; St. Paul, MN; Chicago, IL and Los Angeles County, CA) a total 6814 participants aged between 45 to 84 years were recruited between 2000 and 2002. Participants identified themselves as African-American, Chinese, Hispanic, or White, and were free of clinical CVD at study entry. Each of the 6 field centers recruited approximately the same number of men and women, from at least 2 or more of the racial/ethnic groups included, with sampling designed to achieve a community-representative sample. The study protocol was approved by the institutional review boards of the 6 field centers. Written informed consent was obtained from each participant at study entry.

Study Population

Of the 6814 MESA participants, a total of 87 were excluded from the present analysis: 5 participants with baseline events, 55 with missing data on relevant covariates, and 27 without follow-up information. This defined a final study population of 6727 participants in the present analysis.

Measurement of CAC

All participants underwent CAC scoring at baseline. At the field centers in Chicago, Los Angeles, and New York, CAC was measured using cardiac-gated electron beam computed tomography (CT), whereas at the Baltimore, Forsyth County, and St. Paul field centers CAC was measured using multidetector CT.[19,20] Mean

radiation dose was ≈1 mSv.[21] The images were interpreted in a blinded fashion at the central MESA CT reading center at Harbor UCLA. CAC was quantified using the Agatston scoring method,[22] and the average of the results of 2 consecutive baseline scans was used to determine the baseline CAC score for each study participant.

Measurement of Other Relevant Baseline Covariates

Current smoking status was assessed using a questionnaire and was defined as having smoked cigarettes in the past 30 days relative to the baseline exam. A positive family history of heart attack was defined as self-reported heart attack in a first-degree relative. Blood pressure was recorded as the average of the last 2 of 3 resting systolic blood pressure (SBP) measurements taken in the seated position using a Dinamap model Pro 100 automated oscillometric sphygmomanometer. Lipid and glucose analyses were conducted centrally on aliquots of blood samples drawn from participants after a 12-hour fast to determine levels of total and high-density lipoprotein cholesterol and fasting plasma glucose. Lipid-lowering and hypertension medication use was assessed using a questionnaire and as well as inspection of medication containers. Diabetes mellitus was defined as fasting plasma glucose ≥126 mg/dL or use of glucose lowering medication.

Event Definition and Ascertainment

Participants were contacted every 9 to 12 months through a telephone interview to inquire about new outpatient diagnoses, hospitalizations, and procedures. To date, MESA participants have been followed for a median of 14.2 years. Using established criteria, 2 physicians independently adjudicated events from abstracted medical records.

For the present analysis, all incident CHD events through December 30, 2015 comprised the primary study end point. Identical to the definition used to develop the MESA CHD Risk Score, these were defined as a composite outcome including nonfatal myocardial infarctions, resuscitated cardiac arrest, probable angina, definite angina followed by revascularization, and fatal CHD. Secondary study end points were hard CHD, all CVD, and hard CVD events. Hard CHD included myocardial infarction, resuscitated cardiac arrest and fatal CHD. All CVD was defined as a composite of myocardial infarction, angina-mediated cardiac revascularization, resuscitated cardiac arrest, stroke, or cardiovascular death. Hard CVD included myocardial infarction, resuscitated cardiac arrest, stroke, or cardiovascular death.

Statistical Analysis

Estimation of Average Age- and Sex-Specific Risk Factors of Each Participant's "Healthy Comparator"

Our first step was to define the risk factors of the average age- and sex-specific "generally healthy comparators" who form the basis of our reference comparison. We assumed the healthy comparator was free of diabetes mellitus and current smoking, with otherwise average risk factor values drawn from an overall healthy reference population. For SBP, we excluded participants on hypertension medications and used linear regression models with age, sex, and their interaction term as independent predictors to estimate the mean SBP for each participant's healthy comparator, allowing for the known relationship of SBP and age even within healthy individuals. A similar model was used to predict the mean total cholesterol value for each healthy comparator. For women, spline analyses indicated an inflection point after age 55, and to account for this nonlinear effect of age on cholesterol values, we included a linear spline to accommodate the impact of menopause after middle adulthood. A high-density lipoprotein level of 45 and 55 mg/dL was used for healthy men and women respectively. Also, we calculated the mean background prevalence of treatment with antihypertensive medication, lipid-lowering medication, and having a positive family history of heart attack in the general low to borderline risk MESA subpopulation. These reference risk factor values and background probabilities were entered into the risk calculation of the "healthy comparator."

Estimation of Coronary Age for Each Participant

We used the baseline cardiovascular risk factors of each participant to calculate the 10-year MESA CHD Risk Score with CAC (X1) and without CAC (X2).[23] In addition, the 10-year MESA CHD Risk Score (without CAC) for the healthy comparator ($1–0.99963^{\exp(A)}$, where "A" and 0.99963 are respectively the total terms and baseline survival from the MESA CHD equation) was estimated using values for "healthy" cardiovascular risk factors as described previously, leaving age as unknown. We then equated the 2 risk scores (ie, $X=1–0.99963^{\exp(A)}$) and solved for age. The result is the age at which a participant would have attained his/her current 10-year MESA CHD risk estimation if they had aged with the average levels of cardiovascular risk factors as their healthy comparator.

To illustrate, consider a 60-year-old White man with a family history of CHD, total cholesterol of 200 mg/dL, high-density lipoprotein cholesterol of 45 mg/dL, SBP of 126 mm Hg, and CAC score 220 resulting in

an estimated 10-year CHD risk with CAC of 13% (X1) and without CAC of 8% (X2). In our study, a healthy 60-year-old White man would have an estimated SBP of 123 mm Hg, an estimated total cholesterol of 192 mg/dL, and an estimated high-density lipoprotein cholesterol of 45 mg/dL. Putting these estimated values, along with the average risks previously described into the 10-year MESA Risk Score, yields the equation "A"= (0.0455×Age+2.45). Replacing "A" in $0.13=1-0.99963^{\exp(A)}$ with (0.0455×Age+2.45) and solving for age yields an estimated coronary age with CAC of 76 years. Using a similar approach, the coronary age without CAC would be 65 years.

Description of Coronary Age With and Without CAC

The characteristics of the coronary age distributions and validation of performance of coronary age as a risk estimation tool were approached as follows. We first used locally weighted scatter smoothing (lowess) plots to describe the relationship between estimated 10-year CHD risk (using the MESA CHD Risk Score with CAC) and coronary age by race/ethnicity, separately for men and women. Similarly, we used scatterplots and lowess plots to visually describe the relationship between baseline CAC burden (log transformed as CAC+1) and coronary age, separately for men and women. Also, to visually evaluate how chronological age and coronary age change with increasing baseline CAC burden, box and whisker plots were used, comparing their distributions in participants with a baseline CAC burden of 0, 1 to 99, 100 to 299, and ≥300, respectively. Finally, we also described the distribution of chronological age and of coronary age by sex, race/ethnicity, overall and after stratifying by presence or absence of incident events during follow-up.

Visual Comparison Between Coronary Age and Chronological Age

The difference between coronary age and chronological age (ΔAge) was also calculated. This was done for both coronary age with and without CAC. We then described the distribution of ΔAge using histograms and Kernel density functions, overall, by sex, and for participants with and without incident events during follow-up. Scatterplots were also used to visually describe the relationship between baseline CAC burden (log (CAC+1)) and ΔAge.

Performance of Coronary Age for Risk Prediction

Finally, risk discrimination between incident CHD events and non-events with coronary age (with and without CAC) was evaluated using the area under the receiver operator characteristic curve. For reference comparisons, the C-statistic for chronological age, CHD risk predictions using the MESA CHD Risk Score (with and without CAC), and for CAC alone were also calculated. We paid special attention to the comparison between coronary age and the MESA CHD risk score to confirm that coronary age retained the predictive accuracy of the MESA CHD risk score.

Presentation

A beta version of a combined MESA CHD Risk Score and coronary age application has been developed in order to facilitate easy access to the coronary age method by patients, clinicians, and researchers. There will be an online version and a downloadable app for mobile phones in both "patient" and "clinician" versions. The patient version will be a simple display of the 10-year CHD risk score with their coronary age alongside, and the version for clinicians will in addition present the results without the inclusion of the CAC score in order to demonstrate the effect of considering CAC.

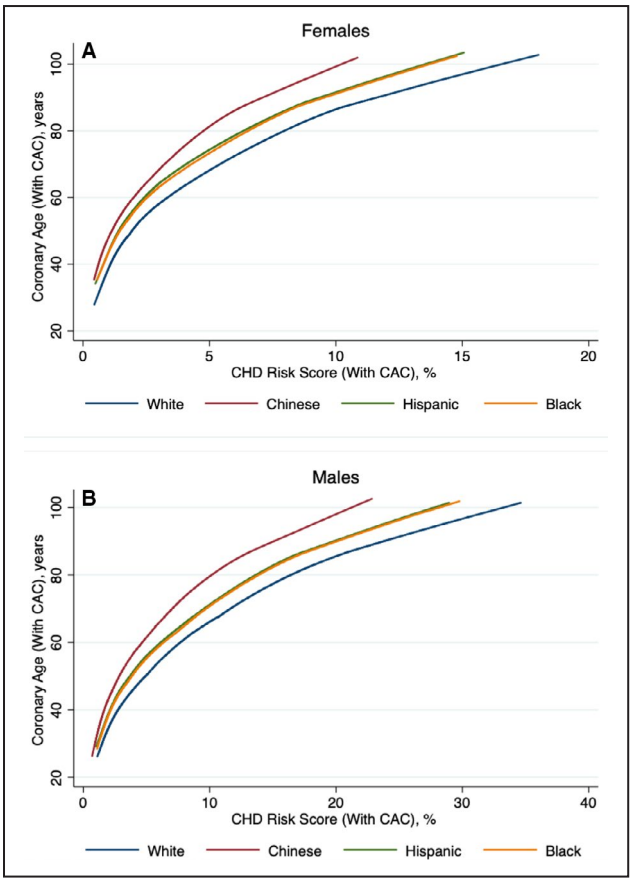

Figure 1. Relationship between 10-year CHD risk estimations using the MESA CHD Risk Score and coronary age (both CAC), by sex and race/ethnicity.
A, Women. **B**, Men. CAC indicates coronary artery calcium; CHD, coronary heart disease; and MESA, Multi-Ethnic Study of Atherosclerosis.

RESULTS

Relationship Between MESA CHD Risk Scores, CAC, and Coronary Age

For both men and women, the MESA CHD Risk Score with CAC and coronary age were positively correlated, with a plot of MESA CHD Risk Score (*x*-axis) and coronary age (*y*-axis) showing a logarithmic shape (Figure 1). For any given MESA CHD risk score the corresponding coronary age was higher for women than for men. By race/ethnicity, for any given MESA CHD risk score the corresponding coronary age was highest in Chinese participants and lowest in White participants, in both men and women.

Figure 2 illustrates the relationship between log-transformed CAC scores and coronary age. In both men and women, coronary age increased linearly with increasing log-transformed CAC scores. For any given CAC score the corresponding coronary age was higher for women than for men.

Figure 3 displays the distribution of chronological age and coronary age (with and without CAC) among subgroups defined by sex and baseline CAC burden. Among individuals with a CAC score of zero, the median of the coronary age with CAC was lower than those for chronological age and coronary age without CAC, particularly among men (Figure 3A). Conversely, among individuals with nonzero CAC scores, median coronary age with CAC was higher than chronological age and coronary age without CAC (Figure 3B through 3D). The largest difference between these distributions was observed for individuals with CAC ≥300, particularly in women.

Coronary Age and Chronological Age Among Individuals With and Without CHD Events

Overall, mean chronological age (62.2 years) was lower than mean coronary age with CAC (63.9 years) and without CAC (66.9 years) (Table 1). Among participants who developed coronary events during follow-up, their chronological age was higher at baseline than that of participants not developing events, and this was true both overall as well as across sex and race/ethnicity strata. Although participants who experienced CHD events during follow-up had higher coronary ages relative to participants who did not experience CHD events, the difference in coronary age between events and nonevents was larger when CAC information was used in the coronary age estimation compared with when CAC was not used (overall difference 18.3 versus 11.6 years).

Distribution of Delta Age Overall and by Incident CHD Events During Follow-Up

ΔAge (ie, the difference between coronary age with CAC and chronological age) appeared normally

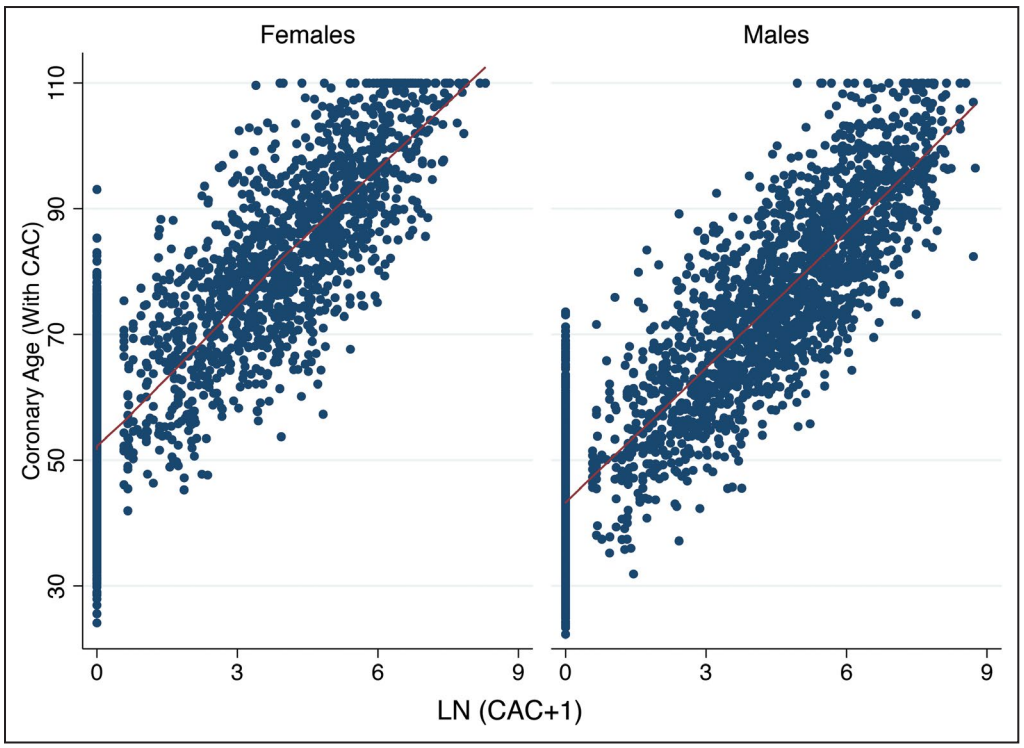

Figure 2. Relationship between CAC and coronary age (with CAC), by sex.
CAC was log-transformed using the natural logarithm of CAC+1. Sex×CAC interaction term is statistically significant (*P*=0.006). Slope for CAC >0: men 7.16 (ln CAC+1), women 7.42 (ln CAC+1). CAC indicates coronary artery calcium; CHD, coronary heart disease; and LN, natural logarithm.

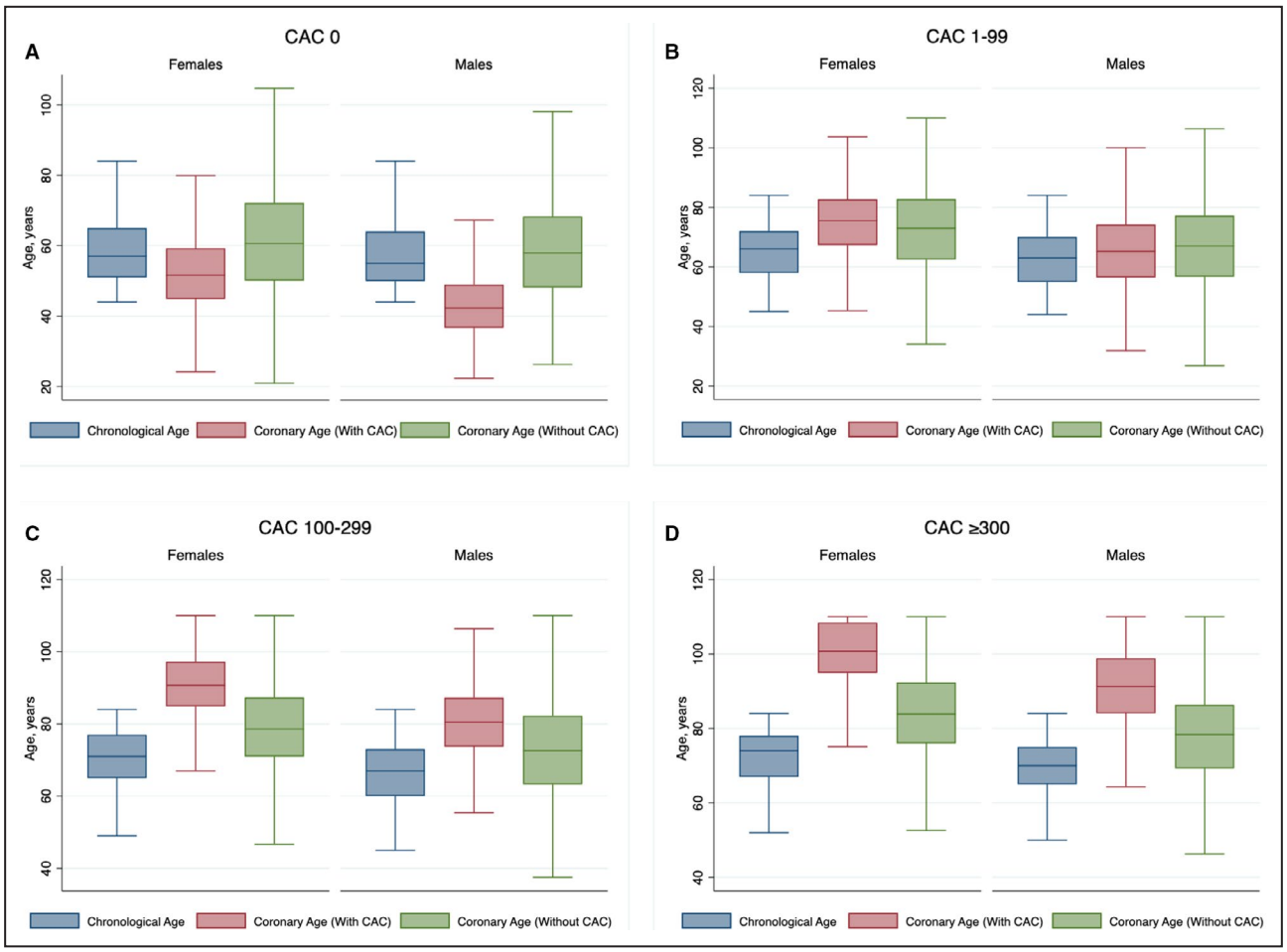

Figure 3. Distribution of chronological age, coronary age with CAC and coronary age without CAC, among CAC strata, by sex.

Comparison of chronological age vs coronary age with CAC, and comparison of chronological age vs coronary age without CAC, significant at $P<0.025$ (corrected for multiple testing) for all CAC strata. **A**, Participants with CAC=0. **B**, Participants with CAC 1 to 99. **C**, Participants with CAC 100 to 299. **D**, Participants with CAC ≥300. CAC indicates coronary artery calcium; and CHD, coronary heart disease.

distributed, with 95% of values ranging from 30 years less than chronological age to 30 years higher than chronological age (Figure S1). The higher the CAC score, the larger the ΔAge with CAC (Figure S2). In general, participants who experienced CHD events during follow-up had a higher coronary age with CAC than their chronological age, whereas most participants surviving free of CHD events had a lower coronary age with CAC as compared with their chronological age (Figure 4A). A similar pattern was seen in the sex-specific plots (Figure S3). On the other hand, differences were smaller between individuals with and without events when CAC was not included in the coronary age estimation (Figure 4B).

Risk Discrimination

Table 2 summarizes the C-statistics for chronological age, coronary age with and without CAC, the MESA CHD Risk Score with and without CAC, and CAC alone for the prediction of incident CHD and CVD events in women and men. In both, the C-statistic for the prediction of CHD events using coronary age with CAC was the same as that of the corresponding MESA CHD Risk Score with CAC from which it was derived (C-statistic of 0.76 in both men and women, the highest across all prediction tools assessed). The coronary age without CAC also had identical C-statistics as those of the MESA CHD Risk Score without CAC (0.72 for women, 0.70 for men), and both of these were lower than those for coronary age with CAC.

An overall, visual comparison of the area under the receiver operator characteristic curves for chronological age and coronary age with and without CAC for the prediction of all CHD events is presented in Figure 5. In the total population, coronary age with CAC showed the best discriminative ability.

Table 1. Distribution of Chronological Age and Coronary Age (With and Without CAC Data) by Sex, Race/Ethnicity, Age, and Incident CHD (All) Events During Follow-Up

	Chronological Age			Coronary Age With CAC			Coronary Age Without CAC		
	All	With Events	Without Events	All	With Events	Without Events	All	With Events	Without Events
Overall	62.2	67.4	61.8	63.9	80.6	62.8	66.9	77.8	66.2
Sex									
Women	62.1	68.5	61.8	64.5	82.4	63.6	67.1	79.9	66.5
Men	62.2	66.7	61.8	63.3	79.5	61.8	66.7	76.5	65.8
Race/ethnicity									
White	62.6	67.6	62.2	62.9	79.6	61.8	66.3	76.1	65.6
Chinese	62.4	71.3	61.9	61.2	85.2	60.0	63.2	80.5	62.3
African-American	62.1	66.4	61.8	66.3	80.0	65.3	69.0	78.2	68.4
Hispanic	61.3	66.7	60.9	64.1	80.4	62.9	67.4	79.0	66.5
Age, y									
45–54	49.7	50.0	49.7	50.7	65.5	50.2	53.0	61.5	52.7
55–64	59.4	59.3	59.4	61.5	78.0	60.7	65.1	74.7	64.6
65–74	69.0	69.0	69.0	71.54	81.9	70.7	75.0	79.7	74.6
75–84	78.2	78.7	78.1	80.9	88.2	79.8	83.4	85.5	83.0

Results are presented as mean. CAC indicates coronary artery calcium; and CHD, coronary heart disease.

DISCUSSION

In this study including 6727 individuals free of overt CVD from MESA, we estimated the "coronary age" of each individual as a function of their MESA CHD risk score to facilitate risk communication, by providing a (biological) coronary age equivalent to the 10-year CHD risk estimate. Among participants who developed CHD events during follow-up, both their chronological age and coronary age at baseline were higher than those of participants not developing events. These differences between individuals with and without events were much larger for coronary age, particularly when CAC information was incorporated in the estimation. Coronary age and the MESA CHD Risk Score (both with CAC) showed identical predictive ability for CHD and CVD events and outperformed chronological age, coronary age and MESA CHD Risk Score (both without CAC), and CAC alone.

Prior studies have evaluated the effectiveness of similar, "risk age" tools for communicating cardiovascular risk to patients. These were found to be easy and intuitive methods enabling patients to better appreciate their cardiovascular risk, potentially motivating them to adopt healthy lifestyle changes to reduce their risk.[13–15,17,24,25] Thus, telling a 45-year-old woman with several risk factors that she has the same cardiovascular risk of a 60-year-old woman with optimal risk factors may be a more effective, change-triggering way to communicate need for improved lifestyle and preventive pharmacotherapies than communicating risk by providing 10-year risk estimations (eg, "your 10-year risk is 10%") or probabilities (eg, "you have a 10% chance of having a major coronary event in the next 10 years"). Although in our study we did not evaluate the impact of coronary age in terms of patient motivation, it may be expected to have similar benefits as those of other similar, biological age-based risk communication tools. We have planned future studies evaluating this assumption.

The methodological approaches used to develop these tools have differed across studies. D'Agostino et al translated the Framingham Risk Score into an equivalent "heart age,"[14] whereas McClelland and colleagues used only CAC data from MESA to derive a simple "arterial age."[13] In contrast, we used the full MESA CHD Risk Score to estimate each participant's "coronary age." This approach takes advantage of the already-validated MESA CHD Risk Score developed using more contemporary data as compared with algorithms such as the Framingham Risk Score or the Pooled Cohort Equations. The MESA CHD Risk Score is more comprehensive and unlike most clinical scores, which are based on only the traditional Framingham cardiovascular risk factors, this score also includes family history of CHD, 4 race/ethnicity categories, and CAC. Our strategy also allowed us to take advantage of the improved predictive accuracy that the MESA Risk Score has demonstrated over other risk scores such as Framingham's, particularly when CAC information is used.[18,26–28] Finally, by using not only CAC data but the whole set of predictors included in the MESA CHD Risk equation we were able to conduct

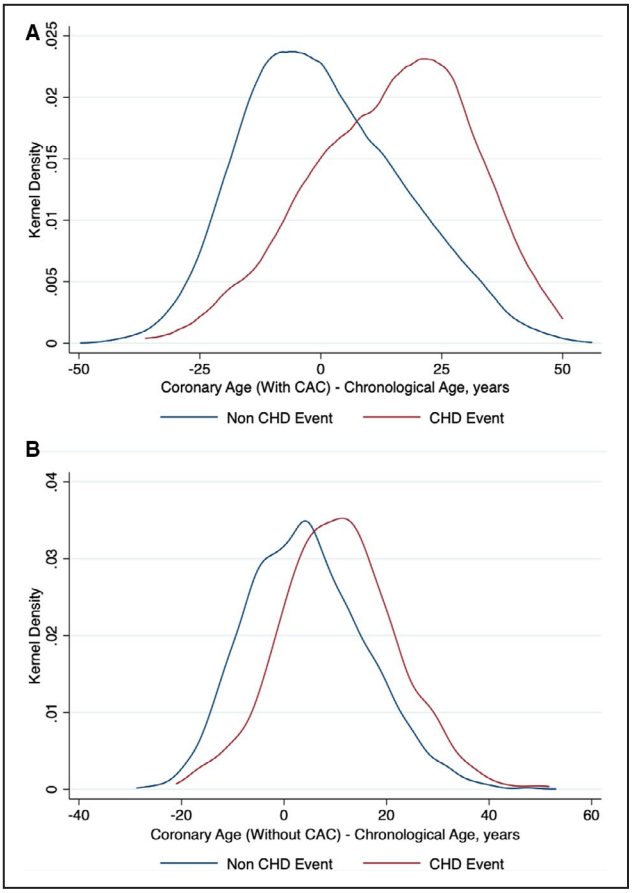

Figure 4. Distribution of ΔAge (ie, coronary age minus chronological age) for participants with and without events during follow-up.
A, Coronary age with CAC. **B**, Coronary age without CAC. CAC indicates coronary artery calcium; CHD, coronary heart disease; and CHDA, coronary heart disease (all).

Table 2. Measures of Discrimination of CHD and CVD Events During Follow-Up Using Chronological Age, Coronary Age (With and Without CAC), MESA CHD Risk Score (With and Without CAC), and CAC Alone, by Sex

	CHD		CVD	
	All	Hard	All	Hard
Women				
Chronological age	0.65	0.68	0.68	0.68
Coronary age (with CAC)	0.76	0.76	0.75	0.73
Coronary age (without CAC)	0.72	0.73	0.73	0.73
MESA Risk Score (with CAC)	0.76	0.76	0.75	0.74
MESA Risk Score (without CAC)	0.72	0.73	0.73	0.73
CAC	0.72	0.71	0.70	0.68
Men				
Chronological age	0.62	0.64	0.64	0.64
Coronary age (with CAC)	0.76	0.74	0.75	0.73
Coronary age (without CAC)	0.70	0.70	0.71	0.71
MESA Risk Score (with CAC)	0.76	0.74	0.75	0.73
MESA Risk Score (without CAC)	0.70	0.70	0.71	0.71
CAC	0.73	0.71	0.71	0.68

Results are presented as area under the ROC curve. CAC indicates coronary artery calcium; CHD, coronary heart disease; CVD, cardiovascular disease; MESA, Multiethnic Study of Atherosclerosis; and ROC, receiver operator characteristic.

a more comprehensive biological age calculation as compared with prior tools developed in MESA.[13]

The results of our analysis suggest that the ability of this new tool of "coronary age" to accurately separate patients who develop CHD events from those who do not is as good as that of the MESA CHD Risk Score. These observations are consistent with the better performance of the MESA CHD Risk Score with CAC as compared with the same score without CAC information.[23] Our results suggest that improved risk communication with coronary age can occur without losing any predictive information compared with MESA CHD Risk Score estimates.

The present findings have important clinical implications. The current mode of predicting and communicating CHD risk in probability terms may prevent patients from fully appreciating their risk, as probabilities are generally difficult to understand.[8,9] This is in spite of the ability to accurately predict CHD risk by some available risk prediction equations, such as the MESA CHD Risk Score. Based on our study, clinicians using the latter to inform risk discussions with patients and shared decision-making may consider also introducing coronary age to further enhance these conversations. A beta version of the coronary age calculator is available, built on the existing MESA CHD Risk Score app (see Apple/iTunes and Android app stores). Web-based apps are currently being developed to facilitate communication (see https://www.mesa-nhlbi.org/CAC-Tools.aspx). Further research on how this approach affects patient risk understanding and implementation of preventive measures is warranted.

Study Limitations

Estimated coronary ages are modestly sensitive to the average risk factors of the healthy comparators that were used in coronary age calculations. In this context, we allowed healthy comparators to have the mean background risks of treatment with antihypertensive medication, lipid-lowering medication, and of having a positive family history of CHD as those observed among the overall, low to borderline risk, "generally healthy" MESA participants. This may have underestimated the difference between chronological and estimated coronary age, which would likely have been larger if we had assumed an optimally healthy, never-treated individual. Nevertheless, given pervasive background treatments

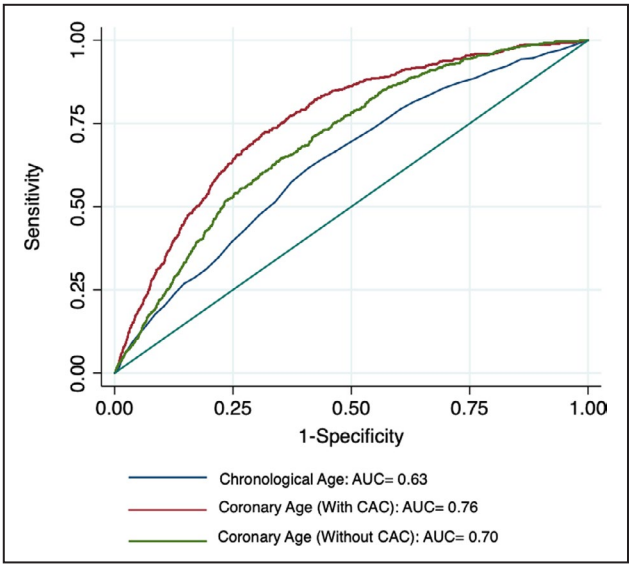

Figure 5. Discrimination of CHD events during follow-up using chronological and coronary age, respectively.
Results are presented as area under the ROC curve. AUC indicates area under the curve; CAC, coronary artery calcium; CHD, coronary heart disease; and ROC, receiver operator characteristic.

in all populations, we believe our approach may be more realistic and therefore relevant to patients, while also optimizing risk calibration (ie, produces a mean overall coronary age nearly equivalent to mean overall chronological age). We tested a variety of alternative definitions of "healthy" comparators, and although these modestly change the absolute value of coronary age (eg, by 1–2 years), they have no impact on ordering of coronary age values and thus no effect on their robust correlation with the MESA CHD Risk Score predictions.

Second, our estimation of coronary age was limited to individuals with ages within the MESA study age range (45–84 years), and therefore does not apply to younger individuals. Of note, it has been suggested that these tools may be particularly helpful in younger individuals with low absolute risk estimations as a consequence of their young chronological age.[29] Future studies in younger cohorts with CAC data available, for instance the CARDIA (Coronary Artery Risk Development in Young Adults) Study or the CAC Consortium, may allow further expansion of the age range in which the coronary age could be derived and subsequently used. Third, our results may not be applicable to other racial/ethnic groups not represented in MESA (eg, South Asians).

Fourth, the MESA CHD Risk Score was developed for the prediction of CHD events and therefore is not encompassing of other CVD events such as stroke. Consequently, coronary age was specifically focused on CHD risk and therefore is not generalizable to total CVD risk.

Fifth, just like the MESA CHD risk score, the coronary age calculation is not meant to show improvement with treatment. For instance, a patient on lipid-lowering medication may have their cholesterol levels improve but the inclusion of lipid medications in the risk estimation of the individual will result in a higher CHD Risk Score. It must be noted that similar to the pooled cohort equation (PCE) or the MESA CHD Risk Score, the coronary age is particularly meaningful in statin-naïve individuals and as a tool to inform preventive therapy allocation.

Finally, because our method was built up as a function of the MESA CHD Risk Score, which was validated in 2 external cohorts showing excellent calibration and discrimination metrics, we did not repeat another external validation study.[23]

CONCLUSIONS

The utility of current CHD/CVD risk scores is potentially hindered by a general difficulty with understanding predicted risk probabilities. In this context, our study suggests that the coronary age, which was developed using data from a contemporary multiethnic cohort and integrating the prognostic information from CAC and several traditional risk factors, may be an accurate translation of the MESA CHD risk estimates into biological age language, while preserving the improved predictive accuracy of the score. An online application built upon the MESA Risk Score (Figure S4) will facilitate access and implementation of this novel method for improved risk communication to patients. Future studies should ensure that there are no unexpected downsides to communicating risk with this approach and should test if the coronary age is an easier to understand and a more effective tool than current risk estimation strategies to promote the adoption of preventive lifestyle and pharmacologic therapies by patients.

ARTICLE INFORMATION

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Supplementary Material

Figures S1–S4

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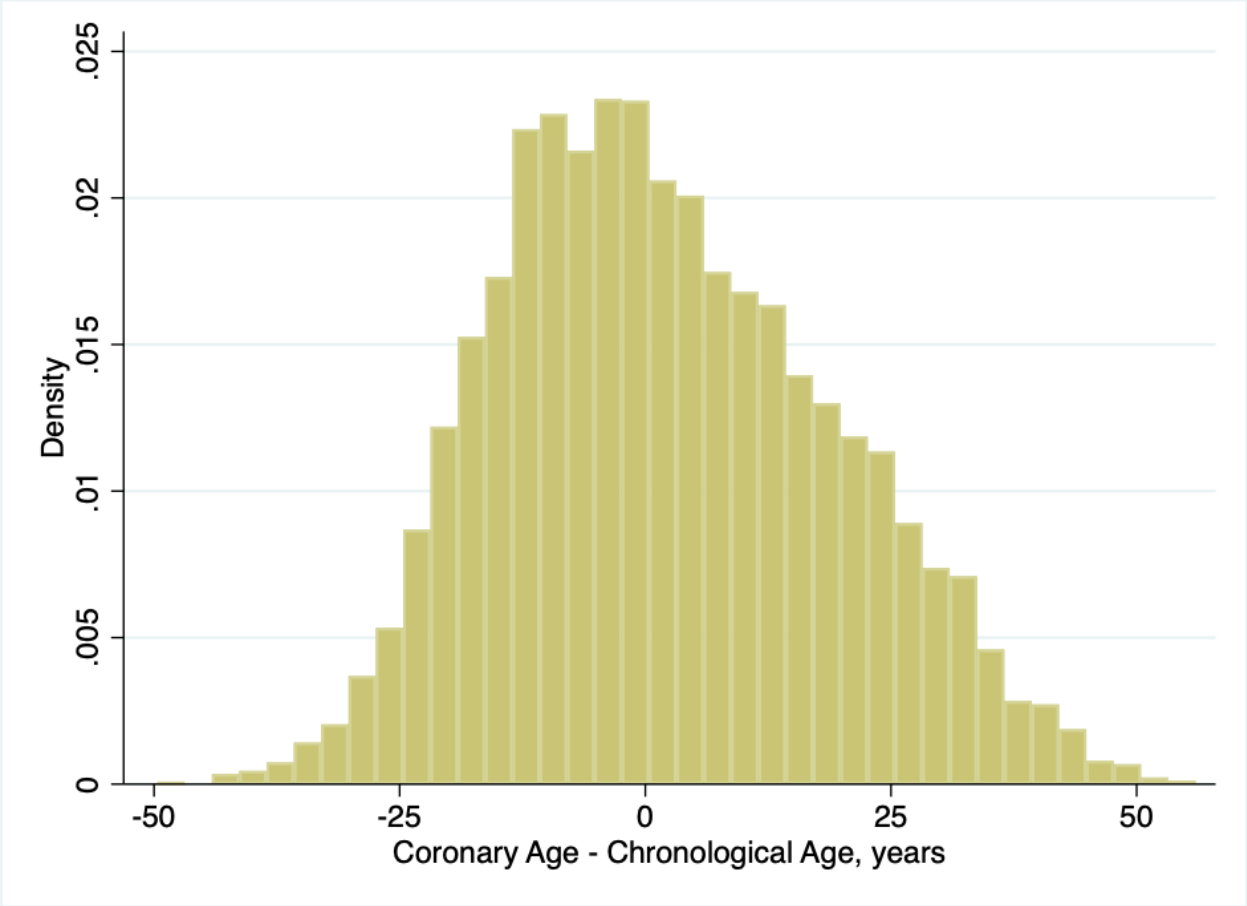
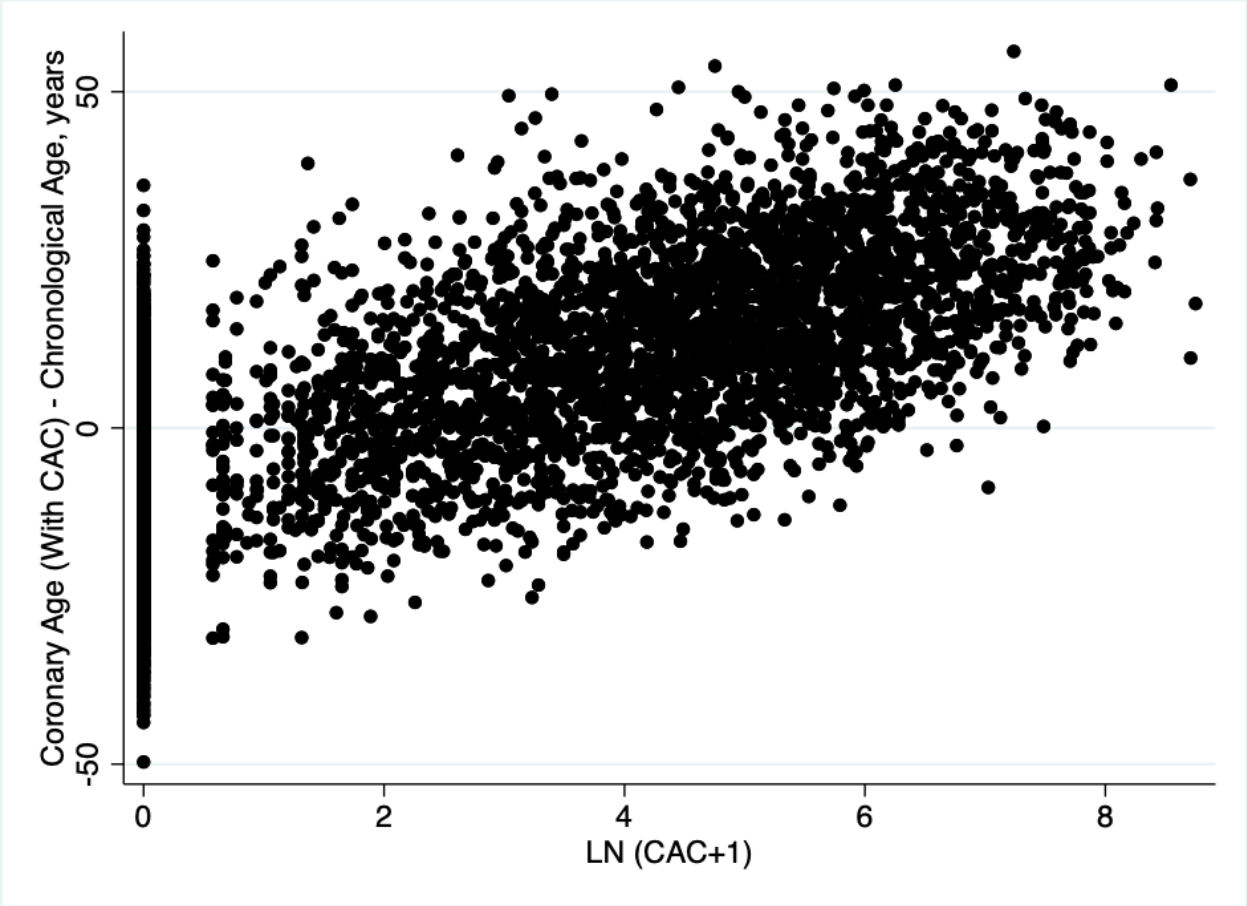
SUPPLEMENTAL MATERIAL

Figure S1. Distribution of ΔAge (with CAC) in the study population.



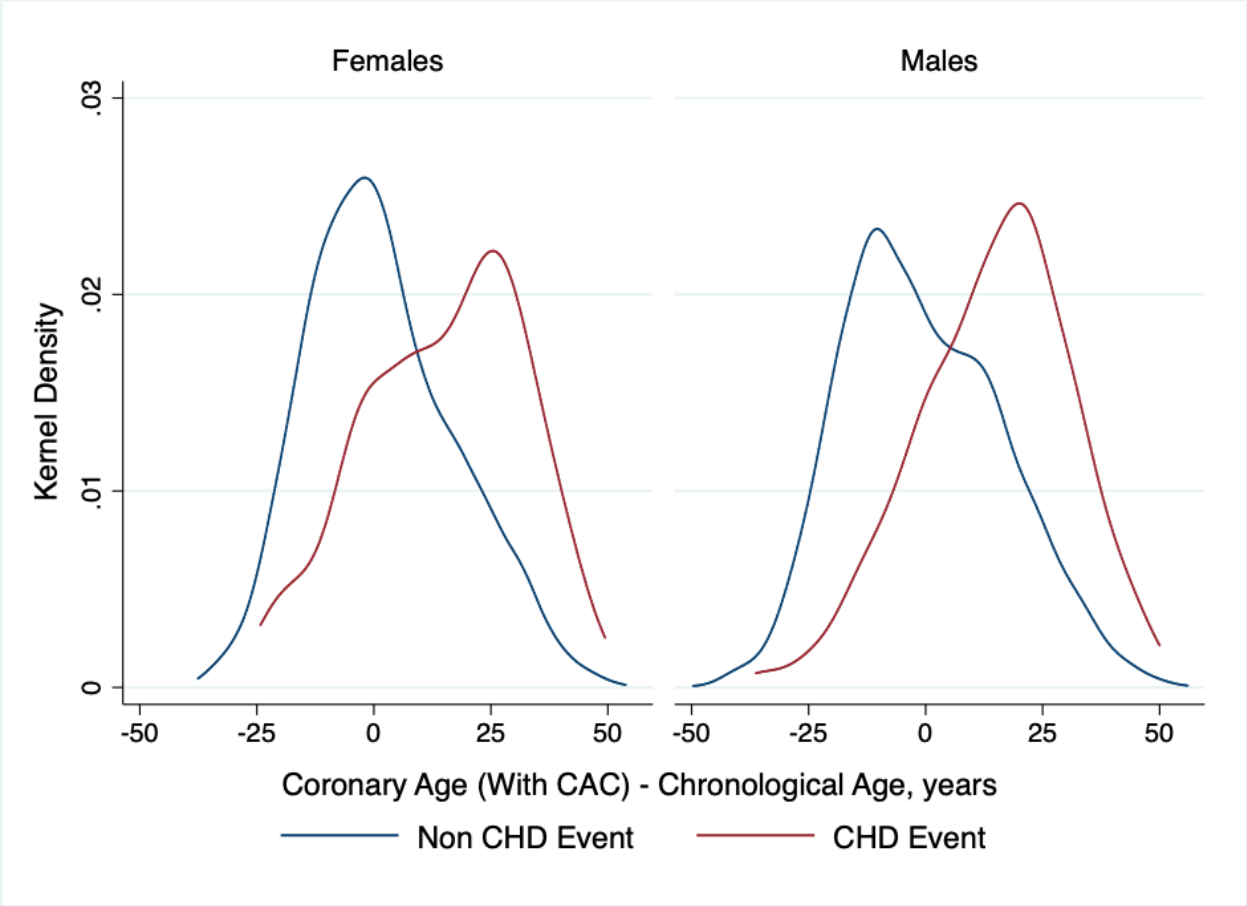
CAC = coronary artery calcium

Figure S2. Relationship between CAC and ΔAge (with CAC).



CAC = coronary artery calcium, LN=Logarithm

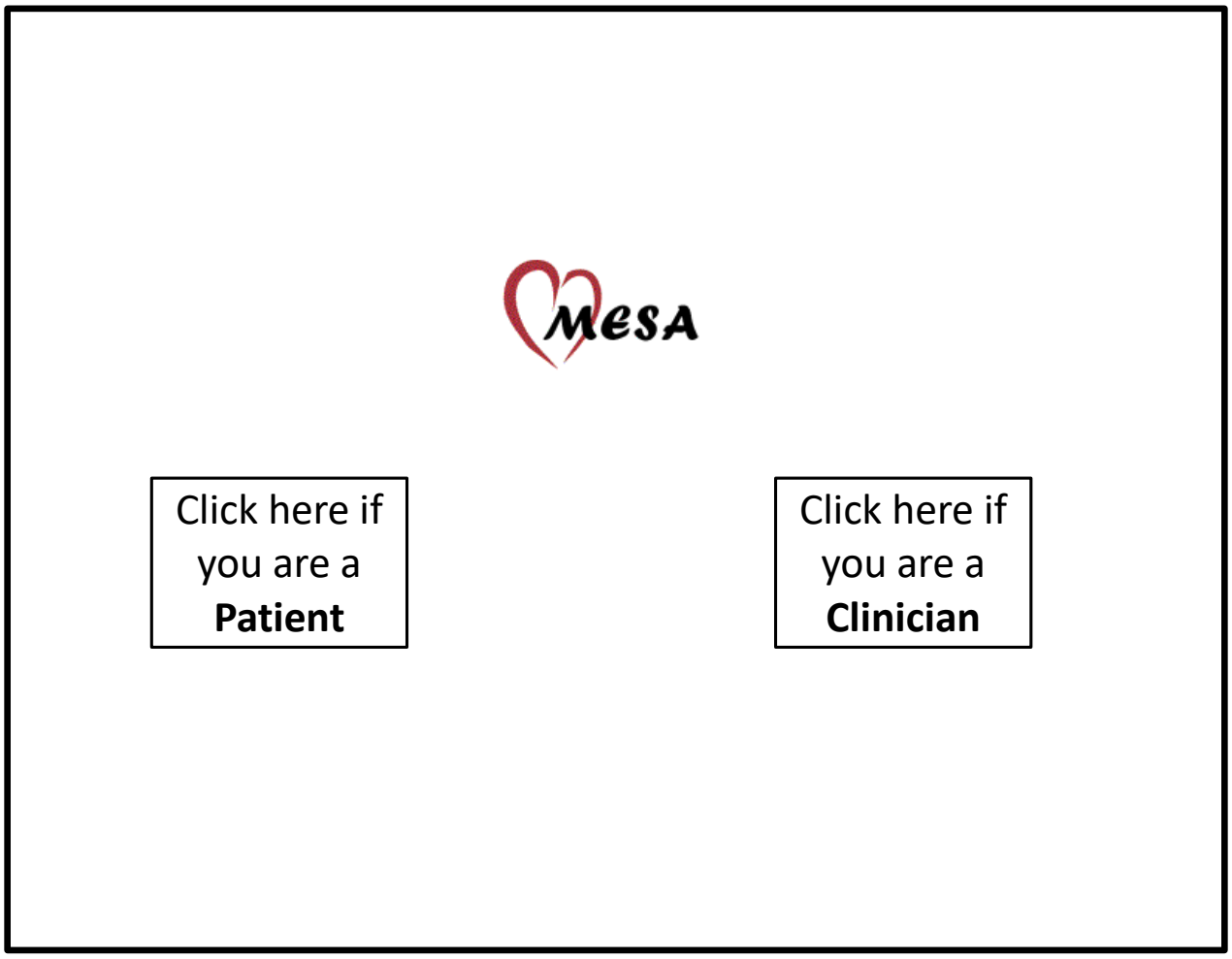
Figure S3. Distribution of ΔAge (i.e., coronary age (with CAC) minus chronological age) for participants with and without events during follow-up, by sex.



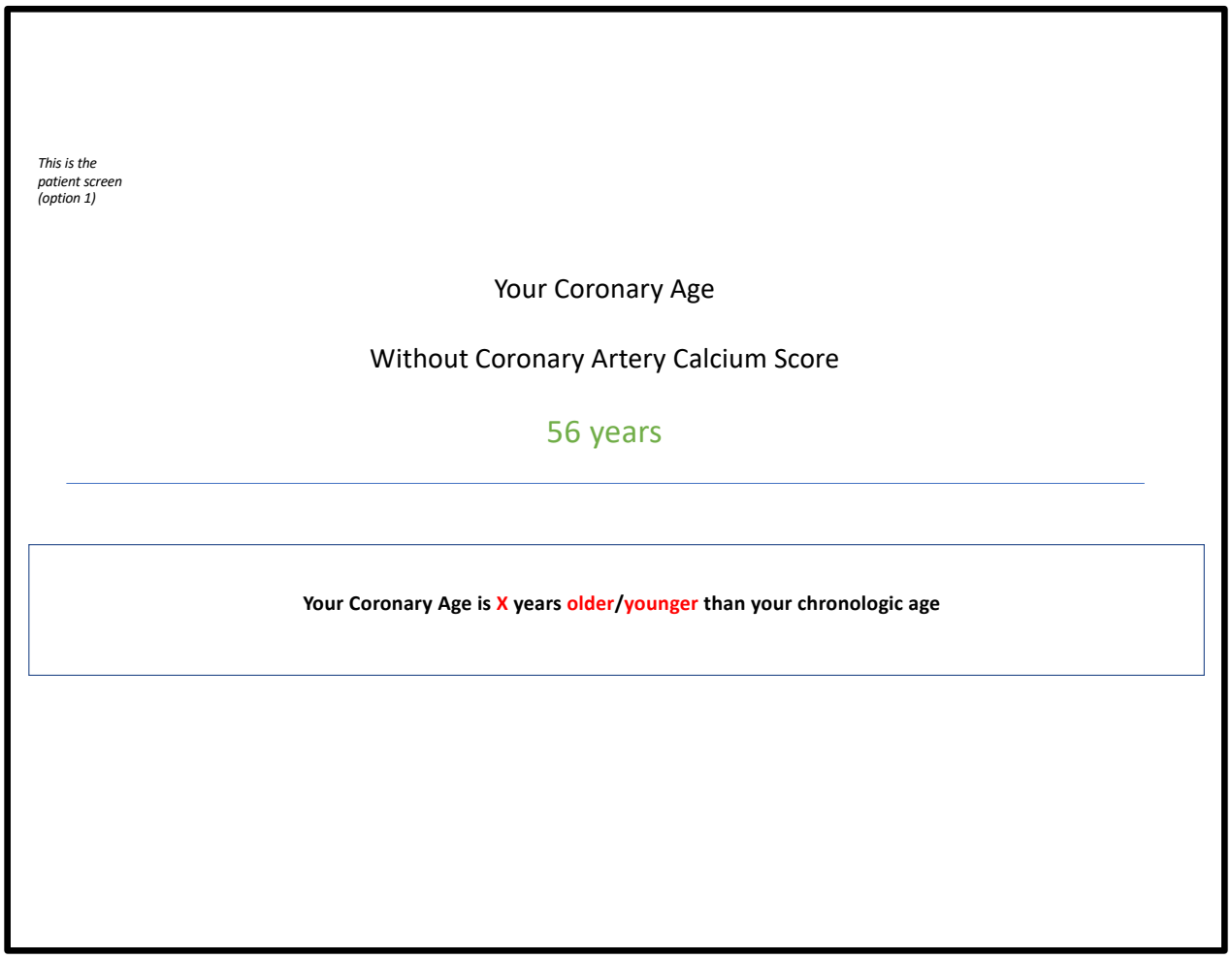
CAC = coronary artery calcium, CHD=Coronary Heart Disease

Figure S4. Patient and clinician versions of coronary age application

Panel A. Patient and clinician options



Panel B. Patient version, coronary age without CAC



Panel C. Patient version, coronary age with CAC

Panel D. Clinician version, coronary age with and without CAC