Published in final edited form as:
J Am Coll Cardiol. 2011 November 8; 58(20): 2076–2083. doi:10.1016/j.jacc.2011.08.022.

The Association of Framingham and Reynolds Risk Scores with Incidence and Progression of Coronary Artery Calcification in the Multi-Ethnic Study of Atherosclerosis

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Abstract

Objectives—To compare the association of the Framingham Risk Score (FRS) and Reynolds Risk Score (RRS) with subclinical atherosclerosis, assessed by incidence and progression of coronary artery calcium (CAC).

Background—The comparative effectiveness of competing risk algorithms for indentifying subclinical atherosclerosis is unknown.

Methods—The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective cohort study of 6,814 participants free of baseline CVD. All participants underwent risk factor assessment, as well as baseline and follow-up CAC testing. We assessed the performance of the FRS and RRS to predict CAC incidence and progression using relative risk and robust linear regression.

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Results—The study population included 5,140 individuals (61±10 years, 47% males, mean follow-up: 3.1±1.3 years). Among 53% of subjects (n=2,729) with no baseline CAC, 18% (n=510) developed incident CAC. Both the FRS and RRS were significantly predictive of incident CAC [RR 1.40 (95% CI 1.29 – 1.52), and RR 1.41 (95% CI 1.30 – 1.54) per 5% increase in risk, respectively] and CAC progression [mean CAC score change 6.92 (95% CI 5.31 – 8.54) and 6.82 (95% CI 5.51 – 8.14) per 5% increase]. Discordance in risk category classification (< or > 10% 10-year CHD risk) occurred in 13.7%, with only the RRS consistently adding predictive value for incidence and progression of CAC. These subclinical atherosclerosis findings are supported by a CHD events analysis over 5.6±0.7 year follow-up.

Conclusion—Both the RRS and FRS predict onset and progression of subclinical atherosclerosis. However, the RRS may provide additional predictive information when discordance between the scoring systems exists.

Keywords

coronary artery calcium progression; subclinical atherosclerosis; risk prediction; Reynolds Risk Score; Framingham Risk Score

Introduction

Coronary heart disease (CHD) is the leading cause of death for men and women in the United States.(1) The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP-III) guidelines recommend that all adults undergo an office-based assessment to evaluate their risk of CHD events, based on the Framingham risk score (FRS).(1) This widely used prediction algorithm incorporates age, gender, levels of total cholesterol, high-density lipoprotein cholesterol (HDL-C), smoking status, systolic blood pressure, and antihypertensive therapy to estimate a 10-year risk for developing a myocardial infarction (MI) or death due to CHD. The ATP-III guidelines set thresholds for lipid treatment based on the 10-year CHD risk estimated by the FRS.

In an effort to improve cardiovascular disease (CVD) risk prediction, the Reynolds Risk Score (RRS) was derived in a cohort of 25,000 healthy U.S. women.(2) The RRS includes traditional risk factors used in the FRS and adds parental family history of premature CHD and high-sensitivity C-reactive protein (hsCRP). This, and a RRS calibrated for men, provided superior prediction of CVD events compared to the FRS model in two studies.(2,3) Notably, the RRS was developed and tested in predominantly non-Hispanic white populations.

The underlying pathophysiology of most CHD events, atherosclerosis, can now be measured non-invasively, including via quantification of coronary artery calcification (CAC) as assessed by computer topography (CT). Identification of individuals with subclinical atherosclerosis, via CAC, has been shown to predict future cardiovascular events in multiple asymptomatic populations, including the young (<40 years), middle aged (50–70 years), elderly (>70 years), men, and women.(4–12) Serial CAC measurements may provide information on disease progression; importantly, CAC progression has been shown to be a powerful predictor of future CVD events.(4,13–15)

Clinical CHD risk assessment scores correlate with the presence and burden of atherosclerosis identified by these non-invasive methods.(14) However, recent studies have suggested the FRS may misclassify both subclinical and clinical CHD risk in some individuals.(16,17) These inaccuracies may be particularly pronounced among women, who rarely have a risk estimate high enough to meet ATP-III treatment thresholds. As a result, some individuals who do not qualify for primary prevention pharmacotherapies may in fact have advanced subclinical atherosclerosis (18,19).

We evaluated the associations of the FRS and RRS with incident and progression of subclinical atherosclerosis, as estimated by CAC, in nondiabetic MESA study participants with emphasize on instances where the scoring systems provided discordant results. The MESA cohort is ideal for studying these relationships due to its large size, gender balance, multi-ethnic composition, serial measures of subclinical atherosclerosis and rigorous assessment of CHD events.

Methods

MESA is a prospective epidemiologic study of the prevalence, risk factors, and progression of subclinical cardiovascular disease in a gender balanced, multiethnic cohort. The study design and methods have been previously published.(20) Briefly, 6,814 participants aged 45–84 who identified themselves as White, African-American, Hispanic, or Chinese were recruited from 6 U.S. communities in 2000–2002. Participants were free of clinical cardiovascular disease (MI, angina, stroke, transient ischemic attack, heart failure, atrial fibrillation, revascularization, valve replacement, pacemaker or defibrillator implantation, or taking nitroglycerin) at enrollment. All participants gave informed consent, and the study protocol was approved by the Institutional Review Board at each site.

Medical history, anthropometric measurements, and laboratory data for the present analysis were assessed as previously described.(20) Parental history of CHD was considered premature as per NCEP ATP-III guidelines (<55 men, >65 women).

FRS was calculated in accordance with NCEP ATP-III guidelines.(1) Since the NCEP ATP-III FRS calculation does not include adults with diabetes(1), participants with diabetes were not included in this study. Additionally, the FRS and RRS algorithms are only applicable for those aged <80(81) years, therefore, participants age 80(81)-85 were assigned a risk as though they were age 79(80). Otherwise, the gender specific RRS was calculated as described by Ridker et al(2,3)

Measurement of Coronary Artery Calcium

Coronary artery calcium was measured using either electron-beam tomography (EBT) (3 sites) or multi-detector CT (3 sites). Participants were scanned twice consecutively and each scan was read by a single trained physician-reader independently at a centralized reading center (Harbor-UCLA Medical Center / Los Angeles Biomedical Research Institute, Torrance, CA). The methodology for acquisition and interpretation of the scans, as well as reproducibility of the readings, has been reported previously.(21) The results from the two

scans were averaged to provide a more accurate point estimate of the amount of calcium present.

Calcium scores were adjusted using a standard calcium phantom that was scanned along with the participant. The phantom contained 4 bars of known calcium density, and was used to calibrate the X-ray attenuation level between measurements conducted on different machines.(22) The presence of CAC was defined as a volume score >0, and a minimum focus of calcification was based on at least 4 contiguous voxels, which resulted in identification of calcium of 1.15 mm3 for the multidetector computed tomography (MDCT) scanners and 1.38 mm3 for the electron beam tomography (EBT) scanners. The nominal section thickness was 3.0 mm for EBT scanners and 2.5 mm for MDCT.

To quantify CAC progression, a second CAC measurement was performed on approximately half the cohort (randomly selected) at a second exam (September, 2002-Feburary, 2004) and on the majority of the remaining subjects at a third exam (March, 2004-October, 2005). A small portion of subjects received their second CAC measurement at exam 4 (October, 2005-February, 2008), while approximately one quarter of participants (randomly selected) received a third CAC measurement at exam 4. CAC progression was calculated between the baseline and latest scan date with an average time between scans of 3.1+1.3 years. CAC progression is known to be highly dependent on time between scans. Given the difference in follow-up duration between subjects, we adjusted for time between scans in our regression model to factor out the importance of this variable.

CHD Events

CHD events consisted of MI, death from coronary heart disease, definite angina; probable angina followed by coronary revascularization, or resuscitated cardiac arrest. Events were recorded over a median follow-up of 5.8 years. At intervals of 9 to 12 months, an interviewer contacted each participant or a family member by telephone to inquire about interim hospital admissions, outpatient diagnoses of CHD and deaths. To verify self-reported diagnoses, copies were requested of all death certificates and medical records for all hospitalizations and outpatient cardiovascular diagnoses. Next-of-kin interviews for out-of-hospital cardiovascular deaths were obtained. MESA was successful in obtaining medical records for approximately 98% of hospitalized CHD events and information on 95% of outpatient cardiovascular diagnostic encounters. Follow-up telephone interviews were completed in 92% of living participants.

Trained personnel abstracted data from medical records reporting possible cardiovascular events. Two physician members of the MESA mortality and morbidity review committee independently classified each event, and if there was disagreement, the full committee made the final classification. The diagnosis of myocardial infarction was based on a combination of symptoms, ECG findings, and levels of cardiac biomarkers. The adjudicators graded angina as definite, probable, or absent based on clinical judgment. Angina required documentation of symptoms distinct from the diagnosis of MI. A classification of definite angina additionally required objective evidence of reversible myocardial ischemia or obstructive coronary artery disease. The reviewers classified deaths from CHD as present or

absent based on hospital records and interviews with families. A more detailed description of the MESA follow-up methods is available at www.mesa-nhlbi.org.

Statistical Analysis

We used chi-square tests for categorical variables and t-test/ANOVA for continuous variables to assess for baseline differences in demographics and cardiovascular risk factors between participants across FRS and RRS categories (<10% & ≥10%).

Changes in CAC were defined in 2 ways as previously described by Kronmal et al; incident CAC, defined as detectable CAC at the follow-up examination (either examination 2, 3 or 4) in a participant free of CAC at baseline; and change in CAC Agatston Score in participants who had detectable CAC at examination 1.(23) The two CAC endpoints were modeled separately. The probability of incident CAC was modeled as a function of covariates using a generalized linear model with log link and binomial error distribution (relative risk regression). Relative risk regression was used rather than logistic regression because the incidence of new calcification was >10%, so the odds ratio would overestimate the relative risk. To estimate the progression of CAC among those with detectable CAC at baseline, we used multivariable adjusted robust linear regression. We performed a robust regression using iteratively reweighted least squares, i.e., assigned a weight to each observation with higher weights given to better behaved observations. Models were adjusted for race, MESA site and follow-up duration.

The practical clinical application of cardiovascular risk score calculation is to categorize individuals into risk categories. Numerous national consensus guideline recommendations are based on risk categories and therefore individuals which have discordant classification based on the risk prediction model used would be most impacted by which prediction model was used to make guideline driven treatment recommendations. Therefore, the groups of individuals that were classified into a different risk category, less than or greater than 10% risk, depending on which risk prediction model was applied (discordant risk score prediction) were evaluated for a difference in the study outcome variables (incident CAC and CAC progression). If the discordant risk prediction group predicted more or less risk than the risk category for which it was being compared to (the concordant higher or lower risk group), and revealed more or less incident CAC and/or CAC progression than predicted by the risk prediction model being evaluated; then we concluded that the model being evaluated added additional predictive information.

Hazard ratios for incident CHD events were calculated using the Cox proportional hazards regression per 5% increase in risk prediction score for both the RRS and FRS. In a similar fashion hazard ratios were calculated for incident CHD events among those with a risk prediction score <10% versus >10% using both the RRS and the FRS. Hazard ratios for incident CHD among those with discoordinate risk score classification were calculated using RRS <10% & FRS<10% as the reference group. The overall diagnostic performance of each risk prediction model to predict CHD as a continuous variable or dichotomous variable was evaluated by comparing c-indexes for each model.

All statistical analyses were completed using STATA software version 9 (TX).

Results

Of the 6,814 MESA participants, 767 were excluded because of missing follow up CAC testing, 684 due to baseline diabetes and 223 because of a missing variable of interest. The final study population included 5,140 individuals with characteristics shown in table 1 (mean age 61±10 years, 47% males, mean follow up: 3.1±1.3 years).

Overall, 53% (n=2729) had no detectable CAC at baseline; of which 18% (n=510) developed incident CAC at follow up exams. Of those with no detectable CAC at baseline 2244 (82%) had FRS<10% & RRS<10%, 109 (4%) had FRS<10% & RRS≥10%, 158 (6%) had FRS≥10% & RRS<10%, 218 (8%) had FRS≥10% & RRS≥10%.

The FRS and the RRS were associated with incidence and progression of CAC of similar magnitude and statistical significance (table 2a&b) when assessed as both continuous (per 5% increase in predicted event rate) and dichotomized variables (below or above 10% risk). Stratification of these results by race reveled relative risk ratios for incident CAC that were similar to the total population; additionally the interaction term for race was not significant in multiple analyses (table 2a). When stratified by gender, the relative risk for developing CAC for those classified as intermediate to high risk (>10%) compared to those classified as low risk (<10%) by the FRS was 2.41 (95% CI, 1.57–3.72) for women and 1.62 (95% CI, 1.16–2.27) for men (p value for interaction=0.07). The respective relative risks by the RRS were 2.50 (95% CI, 1.63–3.41) for women and 2.40 (95% CI, 1.68–3.41) for men (p value for interaction=0.30) (table 2a). Similar gender specific findings were observed for both risk prediction scores when assessed as a continuous variable (table 2a).

Among those with baseline CAC>0, the mean change in CAC score was consistently greater among Caucasians as compared to Chinese, African Americans and Hispanics when evaluated as a continuous or dichotomized variable (above or below a risk prediction of 10% by RRS or FRS) (table 2b). When stratified on gender, the mean incremental change in CAC score for those classified as intermediate to high risk (>10%) compared to those classified as low risk (<10%) by the FRS was 8.69 Agatston units (AU) (95% CI, 0.40–16.89) for women and 18.79 AU (95% CI, 10.85–26.66) for men (p value for interaction=0.39). The respective mean incremental change in CAC score by the RRS were 14.33 AU (95% CI, 6.92–21.73) for women and 23.38 AU (95% CI, 15.43–31.31) for men (p value for interaction=0.72) (table 2b). Differences in the prediction of CAC progression by gender was not observed when applying the FRS or FRS as a continuous variable (table 2b).

Discordance in risk category classification (below or above 10% CHD risk) between the FRS and the RRS occurred in 13.7% of participants. Of those classified with predicted risk <10% by the FRS, 369 (7.2%) were classified as intermediate to high risk (>10%) by the RRS; these participants had a relative risk of 2.41 (95% CI, 1.57–3.72) of developing incident CAC compared to those classified as low risk (<10%) by both scoring systems (table 3). These subjects also had a CAC progression score 19 AU higher (95% CI, 12–26) as compared to those who were classified as low risk by both scoring systems (table 3). Of those classified with predicted risk >10% by the FRS, 336 (6.5%) were classified low risk (<10%) by the RRS; these participants had a relative risk of 0.54 (95% CI, 0.33–0.88) of

developing incident CAC compared to those classified as intermediate to high risk (>10%) by both scoring systems (table 3). These subjects also had a CAC progression score 16 AU lower (95% CI, −30 - (−)1) as compared to those who were classified as intermediate to high risk by both scoring systems (table 3).

Of those classified with predicted risk <10% by RRS, 336 (6.5%) were classified as intermediate to high risk (>10%) by the FRS; these participants had a relative risk of 1.47 that did not meet statistical significance (95% CI, 0.98–2.21) for the development of incident CAC compared to those classified as low risk by both scoring systems (table 3). However, these subjects had a CAC progression score 11 AU higher (95% CI, 3–19) compared to those who were classified as low risk by both scoring systems (table 3). Of those classified with predicted risk >10% by the RRS, 369 (7.2%) were classified low risk (<10%) by the FRS; these participants had no statistical difference in progression of or development of incident CAC when compared to those classified as low risk by both scoring systems [−6, 95% CI (−18 – 7) progression; 0.86, 95% CI (0.52–1.47) incident] (table 3).

Participants with concordant risk prediction classification of intermediate to high (>10%) risk category by both scores had a higher odds ratio for incident CAC and mean change in CAC score than those classified as intermediate to high (>10%) risk by one risk prediction model but low (<10%) risk by the other risk prediction model (table 4).

A total of 135 participants (2.63%) had CHD events during a mean follow-up of 5.6±0.7 years. Adjusting for race, the hazard ratios (95% CI) for any incident CHD event with every 5% increase in FRS and RRS were 1.42 (1.33–1.52) and 1.32 (1.27–1.41), respectively. The relative risk for developing CHD for those with intermediate to high risk (>10%) compared to those considered low risk (<10%) by the FRS was 3.62 (2.57–5.08). The respective relative risk for the RRS was 4.58 (3.24–6.48). The c-indexes for the FRS and RRS for predicting incident CHD events were not significantly different when assessed as either as a continuous variable (0.71 vs. 0.75, p=0.27) or dichotomous variable (0.71 vs. 0.72, p=0.21). Analysis of the 6.5% of subjects classified as low risk by the RRS but high risk (>10%) by the FRS and the 7.2% of subjects classified as low risk by the FRS but high risk (>10%) by the RRS was limited by the low absolute number of CHD events, but consistent with the differences found between these two risk scores in the prediction of subclinical atherosclerosis, as assessed by incident and progression of CAC (table 5). Excluding participants with an age >79 years or who denied a parental history of CVD at exam 1, but reported positive family history at exam 2 did not change the results of the above analyses (data not shown).

Discussion

In this large multi-ethnic cohort, both the RRS and the FRS are predictive of incidence and progression of subclinical atherosclerosis, as measured by CAC. Importantly these results were supported by similar findings for CHD events, underscoring the principle that subclinical atherosclerosis is a precursor for CHD events and that the magnitude of this disease process can be assessed by CAC progression. When evaluated as a continuous variable, the RRS and FRS performed equally well in the prediction of incident CAC and

CAC progression. However, considerable re-classification (13.7%) occurred among the risk models when classified into conventional risk categories, as is done in clinical practice. When classified into low and high-intermediate risk groups, the RRS provided additional predictive power beyond the FRS, both for predicting incident / progression of CAC. The converse was not true: the FRS did not consistently add predictive power beyond the RRS for predicting incident CAC, CAC progression, and incident CHD events. An analysis of discoordinate classification between the RRS and FRS on CHD events revealed similar results as that seen with incident and progression of CAC, however, this analysis was limited by the low number of CHD events currently present in this cohort.

Both the FRS and RRS include gender as a weighted variable. In our cohort, gender specific analyses did not reveal a consistent difference in either risk score's capacity to predict progression or incident CAC based on gender. Both risk prediction scores performed equally across four race groups for predicting incident CAC but predicted significantly greater CAC progression in Caucasians as compared to Chinese, African Americans or Hispanics –a finding the warrants validation in independent cohorts.

The reclassification observed in our cohort was considerably less than the reclassification found in the cohort used to develop and test the RRS; nondiabetic women classified as intermediate risk (10%−20% 10 year risk of a major cardiovascular disease event) by the FRS, would be reclassified with the RRS as follows: 21% women to high-risk (>20% risk) and 24% women would be reclassified as low-risk (<10% risk).(2) Importantly, both the analysis of the cohort used to develop the RRS and this analysis are limited by the fact that these two prediction models differ in that the RRS predicts the composite outcome of MI, ischemic stroke, coronary revascularization, and cardiovascular death whereas the FRS was designed to predict MI and CHD death only. Additional limitations include an upper age limit in the FRS and RRS algorithms of 79 and 80 year respectively, therefore, for participant aged 80(81)-85 we assigned them a risk as though they were age 79(80). Detailed family history was evaluated in MESA at exam 2, whereas baseline CAC was evaluated at exam 1. However, exclusion of subjects > age 79 or who denied a CHD event in any first degree relative at exam 1 but had a positive family history at exam 2 did not change the results of the analysis. Finally, our definition of parental history of CHD is consistent with the NCEP ATPIII guidelines (<55 men, <65 women) but differs slightly from that used in the RRS, (<60 men or women for CHD or stroke). We believe this difference in definitions of family history of CVD is minimal and unlikely to detract from our results.

While robust data exists on the prognostic value of CAC severity in predicting cardiovascular outcomes, less data exist as to whether CAC progression is informative regarding the risk of future events. Multiple studies have demonstrated an association between CAC progression and several traditional and emerging CVD risk factors in this cohort and others.(14,23,24). Emerging data now suggests additive value of CAC progression beyond CAC alone in prediction of CVD events.(4,13–15)

Our study findings raise two important questions. Firstly, do cardiovascular risk prediction models accurately predict the progression of subclinical atherosclerosis? In our study, both the RRS and FRS were significantly associated with progression of subclinical

atherosclerosis as measured by incident CAC and CAC progression. Of particular interest is that this association occurred in an ethnic and gender-diverse population that was unlike the cohort used to develop either risk score. Our incident CHD event data was consistent with the large body of data that demonstrates the association of the FRS and RRS with future cardiovascular events but this study is unique in that it demonstrates that these risk scores also predict progression of subclinical atherosclerosis.

Second, are their differences in RRS and FRS ability to accurately predict progression of subclinical atherosclerosis? Reclassification (13.7%) did occur among the risk models and the RRS provided additional predictive power beyond the FRS, for predicting incident CAC and progression of CAC. This finding of RRS superiority in the prediction of subclinical atherosclerosis was further substantiated with our finding that the RRS had additive value in predicting CHD events in individuals that had discordance between the two risk scores; the same was not true of the FRS.

Conclusion

The RRS and FRS may be useful in predicting the development and progression of subclinical atherosclerosis as assessed by incidence and progression of CAC. When risk classification differences occur between these two risk scoring systems the RRS was more consistently able to provide additional predictive information. The importance of these findings were supported by an analysis of the risk models ability to predict CHD events in this cohort. Further studies are needed to more clearly delineate the role of risk prediction models in identifying subclinical atherosclerosis, and the role of CAC progression in risk prediction and the evaluation of treatment efficacy.

Acknowledgments

This research was supported by R01 HL071739 and contracts N01-HC-95159 through N01-HC-95169 from the National Heart, Lung, and Blood Institute. The authors thank the other investigators, the staff, and the participants of the MESA study for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org

Dr. DeFilippis is supported by a National Research Service Award (NRSA) Training Grant (T32-HL-07227). Dr. Budoff is on the speakers bureau for General Electric (<$10K/year).

Abbreviations

CHD	coronary heart disease
NCEP	National Cholesterol Education Program
ATP-III	Adult Treatment Panel III
FRS	Framingham risk score
CVD	cardiovascular disease
RRS	Reynolds Risk Score
hsCRP	high-sensitivity C-reactive protein

CAC	coronary artery calcification
MI	Myocardial Infarction
AU	Agatston units

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Table 1

Baseline characteristics

Baseline Characteristics	Study Population (n=5140)
Age (years)	61 ±10
Gender (male)	47%
Race Whites	42%
Chinese	12%
African Americans	25%
Hispanics	21%
Family history of heart attack*	9%
Current smokers	12%
Hypertension	41%
Systolic Blood Pressure	125±21
BMI kg/m^2	28±5
Total Cholesterol	195±35
LDL	118±31
HDL	52±15
Trigllycerides median (IQR)	109 (76–157)
hsCRP median (IQR)§	1.8 (0.8–4.1)
CAC€>0	47%
Baseline Volume Score (among those with CAC>0)	230±408
Baseline Agatston Score (among those with CAC>0)	261±491

*Family history defined as a cardiovascular event in a parent <55 male, < 65 female

§high sensitivity C-reactive protein

€Coronary Artery Calcification

Table 2

a: Relative risk of incident CAC associated with increasing risk categories according to FRS & RRS classification. Adjusted for race, MESA site and follow-up duration.

	FRS (continuous***)	RRS (continuous***)	FRS≥10% vs FRS<10%	RRS≥10% vs RRS<10%
Total Population	**1.40 (1.29–1.52)**	**1.41 (1.30–1.54)**	**2.05 (1.58–2.63)**	**2.55 (1.97–3.31)**
Race**				
Caucasians	1.52 (1.39–1.80)	1.53 (1.30–1.79)	2.51 (1.60–3.92)	2.99 (1.90–4.69)
Chinese	1.34 (1.06–1.70)	1.42 (1.15–1.75)	1.89 (0.83–4.29)	2.38 (1.03–5.47)
African Americans	1.34 (1.16–1.54)	1.42 (1.25–1.62)	1.96 (1.25–3.07)	2.61 (1.66–4.10)
Hispanics	1.37 (1.17–1.60)	1.29 (1.08–1.54)	1.75 (1.06–2.89)	2.06 (1.21–3.52)
Interaction for race (P value)	*0.09*	*0.45*	*0.38*	*0.40*
Gender				
Women	1.57 (1.37–1.79)	1.57 (1.38–1.80)	2.41 (1.57–3.72)	2.50 (1.63–3.41)
Men	1.28 (1.15–1.43)	1.30 (1.17–1.45)	1.62 (1.16–2.27)	2.40 (1.68–.41)
Interaction for gender (P value)	*0.006*	*0.01*	*0.07*	*0.30*

b: Mean change in CAC score (Agatston units) associated with increasing risk categories according to FRS & RRS classification. Analysis is robust linear regression, adjusted for race, MESA site and follow-up duration.

	FRS (continuous***)	FRS (continuous***)	FRS<10% vs FRS<10%	RRS≥10% vs RRS<10%
Total Population	6.9 (5.3, 8.5)	6.8 (5.5, 8.1)	17.8 (12.5, 23.0)	21.6 (16.5, 26.8)
Race**				
Caucasians	10.1 (7.2, 13.0)	10.1 (7.8, 12.4)	24.5 (15.3, 33.8)	34.5 (25.5, 43.6)
Chinese	3.9 (0.6, 7.1)	6.0 (3.1, 9.0)	15.7 (5.2,26.2)	17.0 (6.6, 27.4)
African Americans	4.5 (1.2, 7.7)	5.3 (2.6, 8.0)	9.3 (−1.7, 20.2)	20.8 (10.2, 31.3)
Hispanics	5.8 (2.9, 8.7)	2.3 (−0.4, 4.7)	15.3 (6.0, 24.6)	3.0 (−6.6, 12.6)
Interaction for race (P value)	*0.05*	*<0.0001*	*0.03*	*<0.0001*
Gender				
Women	6.2 (3.4, 8.9)	4.4 (2.4, 6.3)	8.7 (0.4, 16.9)	14.3 (6.9, 21.7)
Men	5.9 (3.5, 8.3)	6.5 (4.5, 8.4)	18.8 (10.9, 26.7)	23.4 (15.4, 31.3)
Interaction for gender (P value)	*0.30*	*0.45*	*0.39*	*0.72*

Relative risk ratios (95% CI) were assessed using a generalized linear model and binomial error distribution adjusting for covariates.

** Race not adjusted in multivariable adjusted robust linear regression.

*** for every 5% increase in predicted risk

** Race not adjusted for in multivariable adjusted robust linear regression.

*** change in CAC score for every 5% increase in predicted risk

Table 3

Relative risk of incident CAC and mean change in CAC score with varying FRS and RRS groups according to low and high risk groups classified by FRS and RRS respectively. Adjusted for race, MESA site and follow-up duration.

	Incident CAC Relative Risk Ratio (95% CI)	**CAC Score Change Robust linear regression coefficients (95% CI)**
FRS 10 year CHD risk <10% (n=3847)		
RRS<10% (n=3478)	**1 (ref group)**	**0 (ref group)**
RRS≥10% (n=369) (7.2% discordance)	2.41 (1.57–3.72)	19 (12, 26)
RRS continuous***	1.12 (1.09–1.16)	2.03 (1.50, 2.58)
FRS 10 year CHD risk ≥10% (n=1293)		
RRS <10% (n=336) (6.5% discordance)	0.54 (0.33–0.88)	−16 (−30, −1)
RRS>10% (n=957)	**1 (ref group)**	**0 (ref group)**
RRS continuous***	1.04 (1.00–1.06)	1.01 (0.45, 1.57)
RRS 10 year CHD risk <10% (n=3814)		
FRS<10% (n=3478)	**1 (reference group)**	**0 (ref group)**
FRS≥10% (n=336) (6.5% discordance)	1.47 (0.98–2.21)	11 (3, 19)
FRS continuous***	1.09 (1.06–1.12)	1.88 (1.21, 2.56)
RRS 10 year CHD risk ≥10% (n=1326)		
FRS<10% (n=369) (7.2% discordance)	0.86 (0.52–1.47)	−6 (−18, 7)
FRS>10% (n=957)	**1 (reference group)**	**0 (ref group)**
FRS continuous***	1.02 (0.99–1.05)	0.30 (−0.39, 0.97)

*** for every 1% increase in risk prediction score.

Table 4

Relative risk for incident and mean change in CAC score among participants with discoordinate risk prediction scores. Adjusted for race, MESA site and follow-up duration.

	Incident CAC Scores Relative Risk Ratio (95% CI)	CAC Score Change (AU) Regression coefficient (95% CI)
RRS <10% & FRS<10% (n=3478)	**1 (ref group)**	**0 (ref)**
RRS <10% & FRS≥10% (n=336)	1.48 (0.98–3.72)	13 (3, 23)
RRS >10% & FRS<10% (n=369)	2.42 (1.57–3.72)	22 (14, 31)
RRS ≥10% & FRS≥10% (n=957)	2.74 (2.01–3.72)	24 (17, 29)

Table 5

Hazard ratio for incident CHD among participants with discoordinate risk prediction scores.

	Hazard Ratio for Incident CHD (95% CI)
RRS <10% & FRS<10% (n=3478)	**1 (ref group)**
RRS <10% & FRS≥10% (n=336)	1.91 (0.90–4.04)
RRS >10% & FRS<10% (n=369)	3.65 (2.09–6.39)
RRS ≥10% & FRS≥10% (n=957)	5.47 (3.74–8.00)