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Comparing Risk Scores in the Prediction of Coronary and Cardiovascular Deaths: Coronary Artery Calcium Consortium

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Abstract

Objectives.—To compare risk discrimination for the prediction of coronary heart disease (CHD) and cardiovascular disease (CVD) deaths of the Pooled Cohort Equations (PCE), the Multi-Ethnic

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Study of Atherosclerosis (MESA) Risk Score (with/without coronary artery calcium [CAC]), and of simple addition of CAC to the PCE.

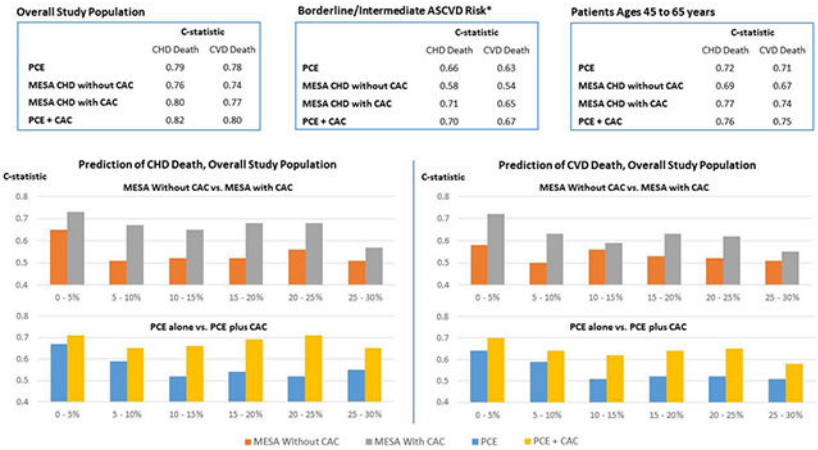
Background.—The PCE predict 10-year risk of atherosclerotic CVD events and MESA Risk Score predicts risk of CHD. Their comparative performance for the prediction of fatal events is poorly understood.

Methods.—We evaluated 53,487 patients ages 45–79 years from the CAC Consortium, a retrospective cohort study of asymptomatic individuals referred for clinical CAC scoring. Risk discrimination was measured using C-statistics.

Results.—Mean age was 57 years, 35% were women, 39% had CAC=0. There were 421 CHD and 775 CVD deaths over a mean 12-year follow-up. In the overall study population, discrimination with the MESA Risk Score with CAC and the PCE was almost identical for both outcomes (C-statistics 0.80 and 0.79 for CHD death, 0.77 and 0.78 for CVD death, respectively). Addition of CAC to the PCE improved risk discrimination, yielding the largest C-statistics. The MESA Risk Score with CAC and the PCE plus CAC showed the best discrimination among the 45% patients with 5-20% estimated risk. Secondary analyses by estimated CVD risk strata showed modestly improved risk discrimination with CAC also among low and high estimated risk groups.

Conclusions.—Our findings support the current guideline recommendation to use, among available risk scores, the PCE for initial risk assessment; as well as to use CAC for further risk assessment in a broad borderline/intermediate risk group. Also, in select individuals at low or high estimated risk, CAC also modestly improves discrimination. Studies in unselected populations are needed to better understand the potential value of tools combining the PCE and CAC for optimal risk assessment.

Graphical Abstract



Keywords

cardiovascular disease; coronary artery calcium; mortality; risk; score

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Introduction

Cardiovascular disease (CVD) risk assessment plays a central role in current international clinical practice guidelines for the allocation of pharmacotherapy in the primary prevention of atherosclerotic CVD (ASCVD). Specifically, guidelines for the appropriate use of statins (1–3), aspirin (2–4), and anti-hypertensive therapy for stage 1 hypertension (5) are explicitly risk-based, and future recommendations for the allocation of other treatments are expected to incorporate risk estimations into physician-patient discussions and decision-making algorithms (6,7). Allocating therapies to patients at the highest risk helps maximize net benefit, both by increasing the yield of treatment in those most likely to benefit as well as by reducing potential harm in low risk patients who are less likely to achieve significant absolute risk reduction.

In 2013, the American College of Cardiology and the American Heart Association (ACC/AHA) released an updated 10-year ASCVD Risk Estimator (the Pooled Cohort Equations [PCE]), inclusive of CHD events and stroke (8). The PCE were also recommended for initial ASCVD risk assessment in the recent 2018 and 2019 guideline updates (1, 4). In parallel, in 2015 researchers from the Multi-Ethnic Study of Atherosclerosis (MESA) published a novel score for the 10-year prediction of CHD events which combined the information provided by traditional risk factors and the coronary artery calcium (CAC) score (9).

CAC has been shown to be the single best predictor of CHD and CVD events (10–12). Currently, ACC/AHA guidelines for the management of cholesterol and for the primary prevention of ASCVD both recommend consideration of CAC for further risk assessment among individuals at intermediate risk in whom risk management is uncertain after using the PCE (1, 4).

To date, no study has rigorously compared risk discrimination across currently available prediction scores and risk assessment strategies. The aim of the present study was thus to assess the predictive ability of three currently available risk scores (the PCE, and the MESA Risk Score with and without CAC) for the prediction of fatal CHD and CVD events, as well as of a simple combination of PCE plus CAC, within the CAC Consortium (13), a very large, multi-center study of patients undergoing clinical CAC scoring for CVD risk stratification, with long-term follow-up for CHD and CVD mortality.

Methods

Study Design

The CAC Consortium is a multi-center, retrospective, real-world cohort study aimed at evaluating the associations between CAC and long-term, cause-specific mortality. Full details of the cohort and study methods have been previously described (13). In brief, the CAC Consortium included 66,636 men and women ≥18 years of age with no major cardiovascular symptoms (e.g., angina) and without known established CVD, undergoing clinical CAC scoring for CVD risk assessment purposes in one of four US centers with longstanding experience in CAC scoring: Cedars-Sinai Medical Center, Los Angeles, CA (years 1998–2010); PrevaHealth Wellness Diagnostic Center, Columbus, OH (years 1999–

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2003); Harbor-UCLA Medical Center, Torrance, CA (years 1991–2008); and Minneapolis Heart Institute, Minneapolis, MN (years 1999–2005).

Comparisons between the CAC Consortium population and NHANES 2001–2002 data, the MESA population, and the Framingham Offspring/3rd Generation population have been published elsewhere (13). Written informed consent for participation in research was collected at the four study centers at the time of CAC scanning. Institutional review board approval for coordinating center activities including death ascertainment and death certificate collection was obtained at the Johns Hopkins Hospital.

Study Population

For the present analysis, all patients included in the CAC Consortium meeting the age criteria of the relevant scores simultaneously were included in the study. Specifically, the PCE were originally targeted at individuals ages 40–79 (8), while the MESA Risk Score was designed for patients ages 45–84 years (9). On this basis, all CAC Consortium participants ages 45–79 years were included in the present analysis.

Two clinically relevant study sub-populations were also pre-specified: 1) individuals at borderline/intermediate estimated risk, defined as a 10-year estimated ASCVD risk ranging 5–20% (1, 4), and 2) individuals ages 45 to 64 years, where a majority of CAC scans are performed in clinical practice in the US (13) (Figure 1).

Baseline Evaluation

Baseline data for the CAC Consortium were gathered between 1991 and 2010 (13). All centers contributed detailed patient information including demographics, CVD risk factors, and CAC scores to a centralized coordinating center. We used information on the following risk factors: age, sex, systolic blood pressure (SBP), hypertension, current smoking, diabetes, total and high-density lipoprotein cholesterol concentration, use of anti-hypertensive therapy, race/ethnicity (which was available in 65% of the study population), any family history of CHD, and use of lipid-lowering therapies (which was available in 26,337 participants, and was assumed to be none otherwise).

CAC Assessment

Details on the CAC assessment and scoring methods used in the CAC Consortium have been reported elsewhere (13). In summary, protocols were consistent across centers, ensuring comparability and facilitating data pooling. Non-contrast cardiac-gated computed tomography scans were performed locally using either electron beam tomography (93% of scans) or multidetector computed tomography (7%). Scans were interpreted locally by experienced readers, and CAC was scored at all sites using the Agatston method (14).

Risk Score Calculation

The PCE include separate equations for White and African-American individuals (8). As recommended in ACC/AHA guidelines, equations for non-Hispanic Whites were applied to the 8.3% of CAC Consortium patients of other, non-White, non-African American race/ethnicities (8). The MESA Risk Score was also calculated for all patients, using the

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equations with CAC information ("MESA with CAC") as well as the equations in which CAC data was not included ("MESA without CAC") (9).

Because in some patients from the CAC Consortium information for specific risk factors was available as binary rather than as continuous data (hypertension yes/no rather than SBP; hyperlipidemia yes/no rather than total and high density lipoprotein cholesterol levels), we used a pre-specified, published imputation algorithm to generate continuous values to be used by the scores (13). These methods have been shown to produce nearly identical mean and median PCE values, with an overall correlation coefficient of 0.952 between scores calculated with original continuous and calculated continuous risk factor data, respectively (13). For both the PCE and the MESA Risk Score, their respective equations for non-Hispanic Whites were used in the 35% participants with missing data on race/ethnicity.

Event Definition and Ascertainment

The outcomes of the present study were CHD death and CVD death (defined as death from CHD, stroke, heart failure, and other cardiovascular causes) assessed over a mean of 12 years. In the CAC Consortium, mortality was assessed via linkage of patient records with the Social Security Administration Death Master File using a previously validated algorithm (15). Cause of death was obtained from the National Death Index, and categorized into common causes of death using International Classification of Diseases, 9th and 10th revisions' codes, as previously described (13).

A detailed comparison of death rates in the CAC Consortium with the U.S. Census and MESA has been previously published (13). Internal validation studies against known deaths identified via the electronic medical record revealed >90% specificity for identifying known deaths, with an estimated sensitivity of 72-90% (13).

Statistical Analyses

Baseline characteristics of the study population were described overall, as well as for the two pre-specified relevant subgroups. For each, the frequency of traditional CVD risk factors was calculated, along with the mean and median CAC score, and the mean 10-year risk estimation provided by each of the scores.

We evaluated the predictive ability of four risk assessment approaches: three currently available risk scores (the PCE alone, the MESA Risk Score without CAC, and the MESA Risk Score with CAC), as well as of the simple combination of the PCE plus CAC (1, 4). Because these scores were originally created to predict different endpoint definitions, for the present analysis using death events we compared the risk scores in terms of risk discrimination, which is their ability to numerically separate events from non-events, rather than calibration. Risk discrimination was calculated using Harrell's C-statistic (16), which is analogous to the area under the receiver-operator characteristic curve but takes into account censoring during follow-up.

All analyses were performed for both CHD death and CVD death in the overall study population, as well as in the subgroups described above. Also, to better understand the comparative discrimination of the scores, in secondary analyses C-statistics were also

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calculated after stratifying patients into risk groups defined per 5% ASCVD risk increments defined using the PCE (8).

Sensitivity analyses were also pursued, excluding 1) patients on baseline lipid-lowering therapy (26% of sample), and 2) participants with missing data on race/ethnicity. All analyses were conducted using Stata software, Version 15 (17). A two tailed p-value of 0.05 was set as the threshold for statistical significance.

Results

Study Population and Baseline Characteristics

The study population comprised 53,487 patients ages 45–79 years (Figure 1). Of these, the majority (N=43,439, 81%) were aged 45–64 years. Using the PCE, 25,054 patients (46.8%) had an estimated <5% 10-year risk, 24,147 (45.2%) had 5–20% risk, and 4,286 (8.0%) had >20% risk.

Mean age was 57.2 years, 35% were women, and 90% of White ethnicity (Table 1). Median CAC score was 10 Agatston Units (interquartile range 0 – 132), and approximately 39% had CAC=0. Individuals ages 45 – 64 years had a lower burden of traditional risk factors than the overall population (except for current smoking), a lower burden of CAC, and their mean estimated CHD and CVD risks were also lower. On the other hand, patients at borderline/intermediate ASCVD risk were older, had a higher burden of traditional risk factors, CAC, and higher mean estimated risks than the overall study population.

Death Events During Follow-Up

After a mean follow-up of 12 years, there were 421 CHD deaths (0.79%) and 775 CVD deaths (1.5 %). Death rates varied by sex, with 330 CHD deaths (0.95 %) and 557 CVD deaths (1.6 %) recorded among men and 91 CHD deaths (0.48%) and 218 CVD deaths (1.2 %) among women.

Risk Discrimination: Comparison of Currently Available Risk Scores

In the overall study population, the MESA Risk Score with CAC and the PCE showed the best discriminative ability for both study outcomes among currently available risk scores (PCE, MESA Risk Score with and without CAC), with very similar C-statistics (0.80 and 0.79, respectively, for CHD death; and 0.77 and 0.78, respectively, for CVD death). On the other hand, MESA without CAC showed the worst performance of the three scores (Table 2).

Among individuals at borderline/intermediate ASCVD risk, the MESA Risk Score with CAC consistently showed the best risk discrimination for both study endpoints among currently available risk scores, the largest being that for CHD death (C-statistic of 0.71, representing a +0.05 improvement compared to the PCE). The same trend was true among individuals 45 to 64 years of age (C-statistic for CHD death of 0.74, representing a +0.03 improvement compared to the PCE).

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Risk Discrimination: Comparison of Risk Assessment Strategies

In the overall study population, risk assessment strategies incorporating CAC information (PCE plus CAC, and MESA Risk Score with CAC) showed better discriminative ability than their equivalents without CAC (PCE alone, and MESA Risk Score without CAC). Specifically, compared to the PCE alone, addition of CAC information improved the C-statistic by +0.03 for the prediction of CHD deaths, and by +0.02 for CVD deaths. Improvements in the C-statistic with addition of CAC information were larger in the subgroups of individuals at borderline/intermediate ASCVD risk and those aged 45 to 64 years. Overall, the best performance across all scores and strategies was observed for the PCE plus CAC, with overall C-statistics of 0.82 for CHD death (95% confidence interval [95% CI] 0.80, 0.84) and 0.80 (95% CI 0.79, 0.82) for CVD death (Table 2).

Sensitivity Analyses

Similar results were observed after excluding patients on baseline lipid-lowering therapy (Table S1). The same was true after excluding participants with missing data on race/ethnicity (Table S2). For all risk scores and subgroups, discrimination for CHD death was better than for CVD death.

Secondary Analyses: Risk Discrimination by 5% ASCVD Risk Strata

Figures 2 and 3 display the results of secondary analyses describing the C-statistics for CHD death and CVD death by estimated ASCVD risk strata. For both endpoints, the MESA Risk Score with CAC and the PCE plus CAC consistently showed the best discriminative ability for all estimated ASCVD risk strata within the 0–30% range. The largest improvements in the C-statistic between each of these strategies and the PCE (without CAC) were observed in the 10–25% estimated risk range, although modest improvements were also observed in lower and higher risk strata (Figure 4).

Discussion

In a large cohort of asymptomatic individuals referred for clinical CAC scoring, among key currently available risk scoring systems the MESA Risk Score with CAC showed similar discriminative ability for the prediction of CHD and CVD death compared to the PCE in the overall study population (age range 45–79 years, across the entire spectrum of baseline estimated ASCVD risk). However, in the subgroup of individuals in whom current ACC/AHA guidelines recommend CAC scoring for further ASCVD risk assessment, i.e., individuals with a 5–20% 10-year estimated ASCVD risk, the MESA Risk Score with CAC showed a better discrimination than the PCE for both outcomes. The same was true among adults ages 45–64, the age subgroup currently most likely to undergo CAC scoring in the US. Simple addition of CAC to the PCE also improved risk discrimination, not only in these subgroups but also in the overall study population, yielding the best performance. Although the largest improvements with CAC-based risk assessment approaches were observed in the 10–25% estimated ASCVD risk range, modest improvements were also observed in lower and higher risk strata.

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To our knowledge, this is the first comprehensive analysis to compare key currently available risk scores and potential risk assessment strategies in a large, contemporary, real-world primary prevention population. Accurate risk prediction remains the cornerstone of therapy choice in primary prevention, and our results have important implications for risk assessment paradigms in routine clinical practice. First, our study lends additional support to recommendations included in current ACC/AHA guidelines (1, 4) for the initial use of the PCE as the preferred among currently existing scores, identifying very low and very high ASCVD risk cases. Also, our findings in the 45% patients in the borderline/intermediate risk stratum are consistent with prior reports indicating that CAC is most useful in this group (18–21), and provide further support to the current guideline recommendation for consideration of CAC scoring for improved risk assessment in borderline/intermediate risk individuals.

Second, our results make an argument for an expanded use of CAC also in select individuals at low and high estimated risk, as CAC may improve risk discrimination in those groups as well. This is consistent with the findings from prior studies (22). It is important to note, however, that the analysis in the intermediate risk subgroup and the secondary analyses by ASCVD risk strata should be interpreted cautiously, and from the perspective of clinical risk prediction. Specifically, because in those analyses the PCE were used to define the risk strata, CAC-based scores added incrementally more to risk prediction, resulting in larger differences in the C-statistic as compared to those observed in the overall analysis spanning adults of the entire spectrum of ASCVD risk. Still, these analyses are highly informative, as they resemble the use of CAC in routine clinical practice, which is typically pursued in patients deemed to benefit from the test and usually happens after clinical risk estimation (1–4).

Third, our results also make a case for the development of novel risk assessment scores combining clinical risk predictors (such as those included in the PCE) and CAC for the prediction of ASCVD events. Moreover, our findings in the overall CAC Consortium cohort suggest that such a score could have a role in the optimized risk assessment of broad populations. It must be noted, however, that the CAC Consortium is a clinical referral cohort, i.e., is comprised by real-world patients referred to CAC scoring by physicians who expected CAC to be particularly informative in those patients. Consequently, studies in unselected populations will help better understand whether ASCVD scores including CAC information could have a value for initial, optimal risk assessment.

In our study, the MESA Risk Score with CAC was markedly superior to the MESA Score without CAC. This suggests that CAC plays the predominant role in improving risk discrimination, rather than other added factors such as family history of CHD. In prior analyses in MESA, which used a similar definition of family history to that used in the CAC Consortium, CAC improved risk assessment in both individuals with and without any family history (23). Importantly, although the ACC/AHA guidelines include family history of premature (rather than any) CVD among the risk-enhancing features to be considered after initial risk assessment (1, 4), prior data suggest that any family history and premature family history perform similarly for the prediction of incident events (24). Our results together with

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prior analyses (11, 12, 23–25) suggest that CAC provides additional prognostic information even after consideration of a patient's family history, as in the MESA Risk Score with CAC.

We also observed that the MESA Risk Score with CAC improved the prediction of CHD mortality more than that of CVD mortality compared to the PCE. This is not surprising, as CAC is known to be a better predictor of CHD events than of CVD events, and the MESA Risk Score is designed to predict CHD (9) – while the PCE predict ASCVD (8). Similarly, addition of CAC to the PCE resulted in a slightly larger improvement in the prediction of CHD deaths as compared to CVD deaths.

Study Strengths

Our study has several strengths, owing to the strengths of the CAC Consortium (13). These include the very large sample size, which maximized statistical power and allowed conducting detailed, clinically relevant subgroup analyses; the inclusion of individuals from several sites, which increases external validity; and inclusion of a wide range of age and baseline estimated risks.

Study Limitations

Our study also has some limitations. First, imputation techniques had to be used for some SBP and cholesterol levels for risk calculations. However, we have previously shown that imputed data based on diagnoses and treatment of hypertension and dyslipidemia produces highly similar risk score results (13). In addition, this limitation would be expected to impact all scores to a similar extent (as each of the risk scores uses these values), and our prior analyses suggest that the effects of this on the comparative analysis should be small.

Second, information on prior statin use was available in a limited number of participants. Nevertheless, this would be expected to be small in a clinical referral population undergoing CAC scoring for risk assessment. Presence of some statin users in the CAC Consortium population would be expected to favor the MESA Risk Score, which is the only one capturing statin use. However, the results of the sensitivity analysis excluding participants known to be statin users at baseline yielded consistent results with those from the main analysis.

Third, information on pharmacological/invasive treatments of patients after CAC scoring, which may impact the natural history of CHD and CVD, was not available. Nevertheless, this limitation would be expected to impact all scores to a similar extent. Fourth, we evaluated cause-specific mortality as the study outcome, while the risk scores were designed to predict varying definitions of CHD and CVD (both non-fatal and fatal). Nonetheless, mortality is the ultimate "hard" outcome, as its use eliminates the potential biases derived from adjudication of softer CHD and CVD endpoints and may represent an optimal outcome for performing direct comparisons across scores.

Fifth, the proportion of women and of non-White participants was relatively low, which could potentially limit generalizability. However, CAC has shown to be similarly predictive in both men and women as well as across the racial/ethnic groups included in MESA (26). Finally, due to limitations inherent to vital status ascertainment in the US, mortality in the

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CAC Consortium may be underestimated by up to 15-30% (13). Nonetheless, while this would affect an analysis of risk score calibration (observed vs. predicted event rates), it should not differentially affect analyses of risk score discrimination.

Conclusions

Our study in a very large clinical cohort of primary prevention patients undergoing CAC assessment for risk stratification suggests that the PCE should be, among currently available scores, the risk score of choice for initial risk assessment, as recommended in current ACC/AHA guidelines. In patients at 5 to 20% estimated 10-year ASCVD risk, CAC (combined with PCE estimations should this tool be developed, as part of the MESA Risk Score, or alone) improves the prediction of both CHD death and CVD death, and should be considered as a key tool for further, improved risk assessment. In addition, in select individuals at low or high estimated risk, CAC also modestly improves risk discrimination. Ongoing studies in unselected populations are needed to better understand the potential value of novel tools combining the PCE and CAC for optimal risk assessment in even broader populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

ACC/AHA	American College of Cardiology/American Heart Association
ASCVD	atherosclerotic cardiovascular disease events
CAC	coronary artery calcium
CHD	coronary heart disease
CI	confidence interval
CVD	cardiovascular disease
MESA	Multi-Ethnic Study of Atherosclerosis
SBP	systolic blood pressure

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PERSPECTIVES

Clinical Competencies

Because the MESA Risk Score with CAC did not improve global risk prediction in the broad population ages 45–79 years (***Medical Knowledge***), our results lend support to the 2018 and 2019 ACC/AHA guideline recommendation for the initial use of the PCE as the preferred first-line risk score to identify very low and very high risk cases, followed by use of CAC testing in those at borderline to intermediate risk (***Patient Care and Procedural Skills***). In addition, our results suggest that CAC may also improve risk prediction amongst select low and high risk patients.

Translational Outlook

Studies in unselected populations are needed to better understand whether CAC scoring could be expanded to even broader populations for initial, optimal risk assessment as part of novel ASCVD risk assessment scores.

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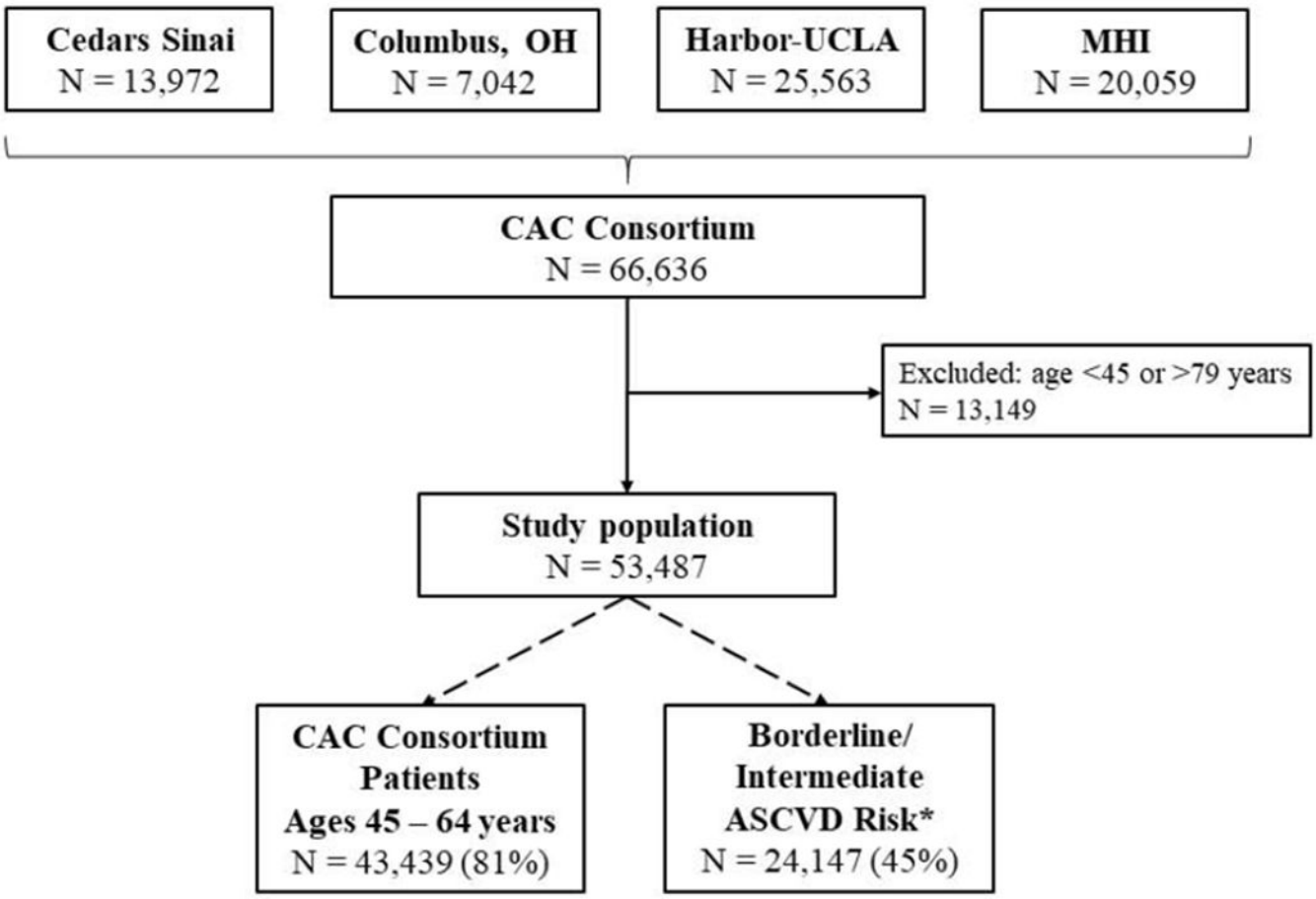

Figure 1. Flow of the population included in the study.

CAC Consortium participants included in the present analysis. *Defined as a 5–20% 10-year estimated ASCVD risk using the PCE.

*Defined as a 5 – 20% 10-year estimated ASCVD risk using the PCE

ASCVD = atherosclerotic cardiovascular disease; CAC = coronary artery calcium; MHI = Minneapolis Heart Institute; OH = Ohio; UCLA = University of California, Los Angeles; PCE = Pooled Cohort Equations

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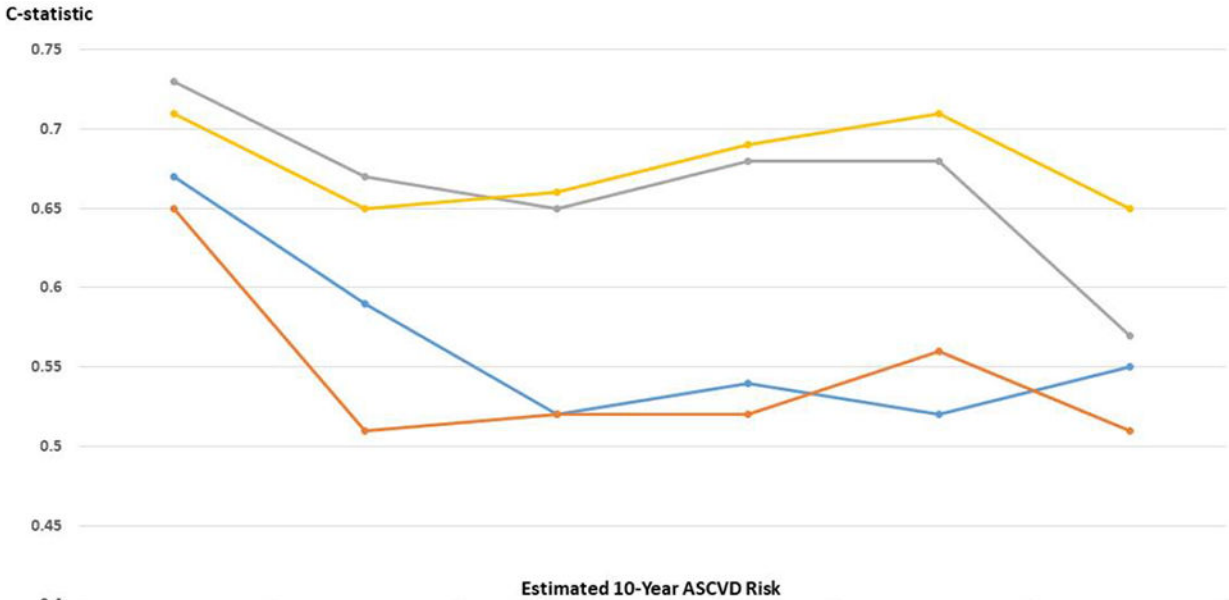

	0 - 5%	5 - 10%	10 - 15%	15 - 20%	20 - 25%	25 - 30%
PCE	0.67	0.59	0.52	0.54	0.52	0.55
MESA Without CAC	0.65	0.51	0.52	0.52	0.56	0.51
MESA With CAC	0.73	0.67	0.65	0.68	0.68	0.57
PCE + CAC	0.71	0.65	0.66	0.69	0.71	0.65

Figure 2. Discriminative ability for the prediction of CHD death events, by 5%-ASCVD risk strata.

Results are presented using the C-statistic.

ASCVD = atherosclerotic cardiovascular disease events; CAC = coronary artery calcium; CHD = coronary heart disease; MESA = Multi-Ethnic Study of Atherosclerosis; PCE = Pooled Cohort Equations

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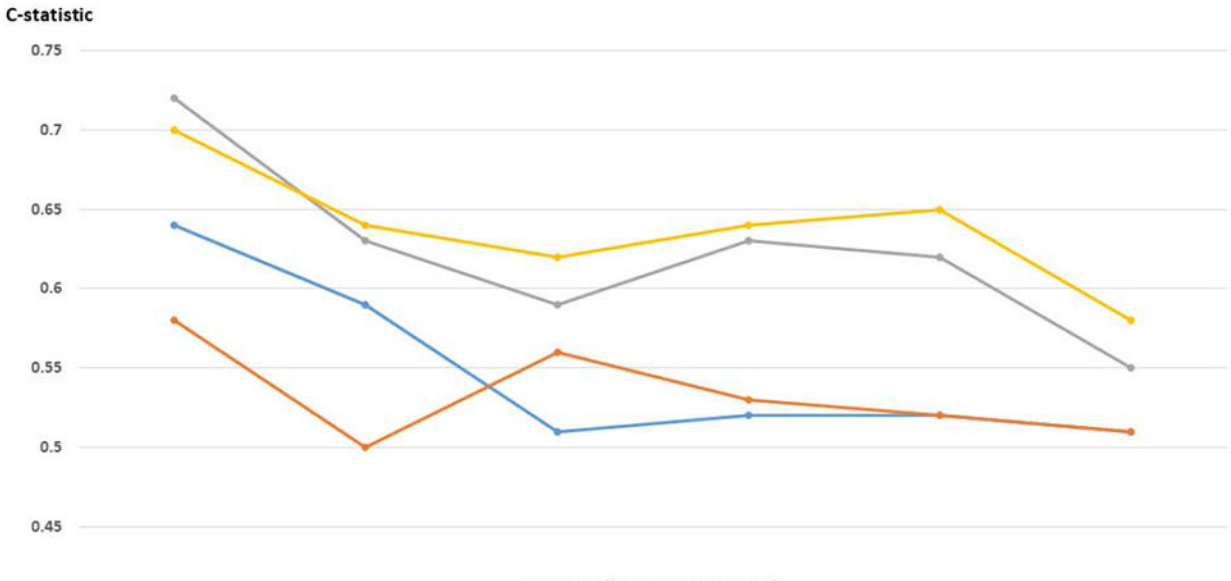

	0 - 5%	5 - 10%	10 - 15%	15 - 20%	20 - 25%	25 - 30%
PCE	0.64	0.59	0.51	0.52	0.52	0.51
MESA Without CAC	0.58	0.5	0.56	0.53	0.52	0.51
MESA With CAC	0.72	0.63	0.59	0.63	0.62	0.55
PCE + CAC	0.7	0.64	0.62	0.64	0.65	0.58

Figure 3. Discriminative ability for the prediction of CVD death events, by 5%-ASCVD risk strata.

Results are presented using the C-statistic.

ASCVD = atherosclerotic cardiovascular disease events; CAC = coronary artery calcium; CVD = cardiovascular disease; MESA = Multi-Ethnic Study of Atherosclerosis; PCE = Pooled Cohort Equations

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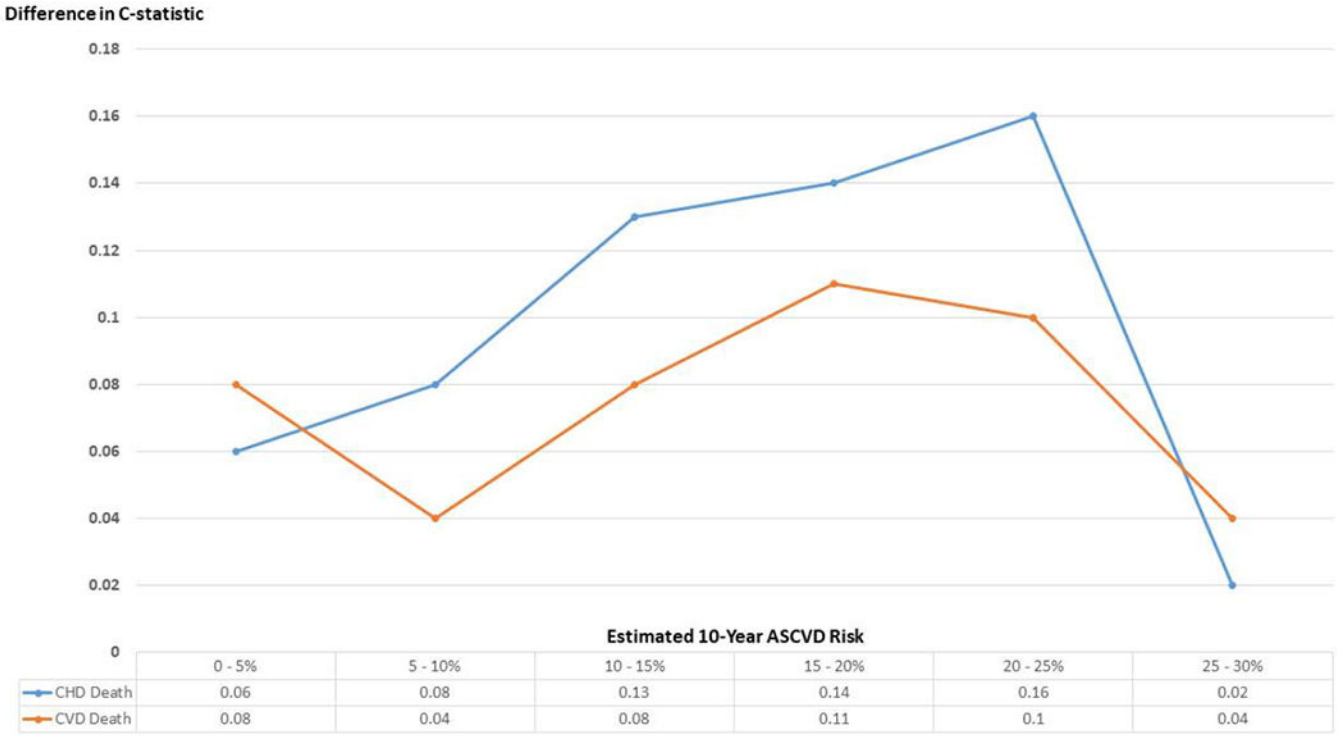

Figure 4. Improvement in the C-statistics for CHD death events and for CVD death events comparing the MESA Risk Score with CAC and the PCE (Panel A), and comparing the PCE plus CAC and the PCE alone (Panel B).

Results are presented as difference in the C-statistic.

ASCVD = atherosclerotic cardiovascular disease events; CAC = coronary artery calcium; CHD = coronary heart disease; CVD = cardiovascular disease; MESA = Multi-Ethnic Study of Atherosclerosis; PCE = Pooled Cohort Equations

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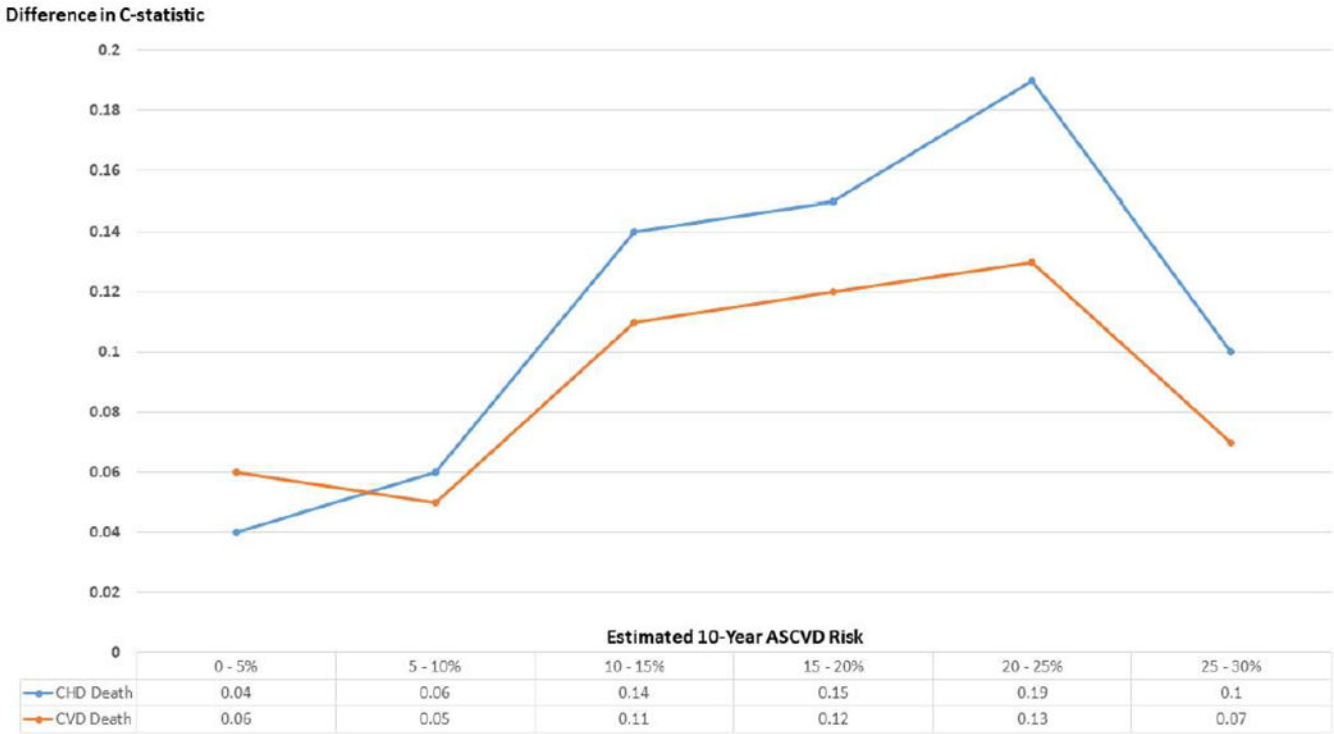

Central Illustration. Discriminative ability of the PCE, the MESA Risk Score (with and without CAC), and of the PCE plus CAC, for the prediction of CHD death and CVD death events in the CAC Consortium.

Results are presented using the C-statistic. On the upper panels, results for all CAC Consortium participants included (overall), for participants at borderline/intermediate estimated ASCVD risk, and for participants ages 45 to 65 years at baseline. On the lower panels, results are presented for all CAC Consortium participants by estimated 10-year ASCVD risk strata.

ASCVD = atherosclerotic cardiovascular disease events; CAC = coronary artery calcium; CHD = coronary heart disease; CVD = cardiovascular disease; MESA = Multi-Ethnic Study of Atherosclerosis; PCE = Pooled Cohort Equations

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Table 1.

Baseline characteristics of the study population, CAC Consortium ages 45 to 79 years.

	Overall Study Population (N=53,487)	Pre-specified relevant subgroups	
		Patients Ages 45 to 64 years (N=43,439)	Borderline/Intermediate ASCVD risk* (N=24,147)
Age, years	57.2 (8.0)	54.2 (5.3)	60.2 (6.5)
Women	18,801 (35.2)	14,733 (33.9)	5,440 (22.5)
Race/ethnicity			
Non-Hispanic White	31,334 (89.7)	25,169 (89.6)	14,045 (88.8)
African-American	775 (2.2)	601 (2.2)	499 (3.2)
Asian	1,241 (3.6)	991 (3.6)	513 (3.3)
Hispanic	1,018 (2.9)	841 (3.0)	477 (3.0)
Other	583 (1.8)	481 (1.7)	275 (1.7)
Hypertension	17,874 (33.4)	13,147 (30.3)	10,009 (41.5)
Use of antihypertensive therapy	2,504 (24.5)	1,586 (19.9)	1,315 (30.1)
Dyslipidemia	29,768 (55.7)	23,674 (54.5)	15,742 (65.2)
Use of lipid-lowering therapies (N=26,337)	6,716 (25.5)	5,102 (23.4)	3,163 (28.1)
Diabetes	3,969 (7.4)	2,839 (6.5)	2,055 (8.5)
Family History of CHD (any)	24,150 (45.2)	19,969 (46.0)	10,441 (43.2)
Current smoking	4,989 (9.3)	4,241 (9.8)	3,399 (14.1)
CAC Score			
Mean, AU	185.5 (499)	126.9 (379.2)	239.4 (529.8)
Median, AU	10 (0 – 132)	3.1 (0 – 79)	41 (0 – 232)
CAC = 0	20,803 (38.9)	19,073 (43.9)	6,176 (25.6)
CAC 1 –100	17,526 (32.8)	14,591 (33.6)	8,756 (36.3)
CAC 100 – 400	8,459 (15.8)	6,009 (13.8)	5,130 (21.2)
CAC > 400	6,699 (12.5)	3,766 (8.7)	4,085 (16.9)
Estimated 10-Year Risk, %			
PCE (ASCVD)	8.1 (7.8)	5.6 (4.5)	10.0 (3.9)
MESA Without CAC (CHD)	5.8 (4.3)	4.9 (3.1)	6.9 (2.8)
MESA With CAC (CHD)	6.9 (6.8)	5.7 (5.6)	8.5 (6.2)

*Defined as a 5 – 20% 10-year estimated ASCVD risk using the PCE

Data presented as number (%), mean (standard deviation) or median (interquartile range)

Percentages may not add 100% due to rounding

Abbreviations: ASCVD = atherosclerotic cardiovascular disease events; AU = Agatston Units; CAC = coronary artery calcium; CHD = coronary heart disease; MESA = Multi-Ethnic Study of Atherosclerosis; N = number; PCE = Pooled Cohort Equations

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Table 2.

Discriminative ability for the prediction of CHD death and CVD death events, overall and in clinically relevant subgroups.

	C-Statistic	
	CHD Death	**CVD Death**
Overall study population		
PCE	0.79 (0.77, 0.81)	0.78 (0.77, 0.80)
MESA without CAC	0.76 (0.74, 0.78)	0.74 (0.72, 0.76)
MESA with CAC	0.80 (0.78, 0.82)	0.77 (0.76, 0.79)
PCE + CAC	0.82 (0.80, 0.84)	0.80 (0.79, 0.82)
Intermediate ASCVD risk (5-20%) *		
PCE	0.66 (0.62, 0.69)	0.63 (0.60, 0.66)
MESA without CAC	0.58 (0.54, 0.62)	0.54 (0.51, 0.57)
MESA with CAC	0.71 (0.67, 0.74)	0.65 (0.62, 0.68)
PCE + CAC	0.70 (0.67, 0.74)	0.67 (0.64, 0.69)
Ages 45 – 64 years		
PCE	0.72 (0.68, 0.75)	0.71 (0.69, 0.74)
MESA without CAC	0.69 (0.66, 0.73)	0.67 (0.64, 0.70)
MESA with CAC	0.77 (0.74, 0.81)	0.74 (0.72, 0.77)
PCE + CAC	0.76 (0.73, 0.80)	0.75 (0.73, 0.78)

* Defined as a 5 – 20% 10-year estimated ASCVD risk using the PCE

Abbreviations: ASCVD = atherosclerotic cardiovascular disease events; CAC = coronary artery calcium; CHD = coronary heart disease; CVD = cardiovascular disease; MESA = Multi-Ethnic Study of Atherosclerosis; PCE = Pooled Cohort Equations