Title

Defining Demographic-specific Coronary Artery Calcium Percentiles in the Population Aged ≥75: The ARIC Study and MESA

Journal

Circulation Cardiovascular Imaging, 16(9)

ISSN

1941-9651

Authors

Wang, Frances M
Cainzos-Achirica, Miguel
Ballew, Shoshana H
et al.

Publication Date

2023-09-01

DOI

10.1161/circimaging.122.015145

Peer reviewed

HHS Public Access

Author manuscript

Circ Cardiovasc Imaging. Author manuscript; available in PMC 2024 September 01.

Published in final edited form as:

Circ Cardiovasc Imaging. 2023 September ; 16(9): e015145. doi:10.1161/CIRCIMAGING.122.015145.

Defining demographic-specific coronary artery calcium percentiles in the age 75-and-older population: The Atherosclerosis Risk in Communities (ARIC) Study and Multi-Ethnic Study of Atherosclerosis (MESA)

Frances M. Wang, PhD, MS[1], **Miguel Cainzos-Achirica, MD, PhD, MPH**[1,2], **Shoshana H. Ballew, PhD**[1], **Josef Coresh, MD, PhD**[1], **Aaron R. Folsom, MD**[3], **Candace M. Howard, MD, PhD**[4], **Wendy S. Post, MD, MS**[1], **Lynne Wagenknecht, DrPH**[5], **Matthew J. Budoff, MD**[6], **Michael J. Blaha, MD, MPH**[1], **Kunihiro Matsushita, MD, PhD**[1]

[1]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

[2]Division of Cardiovascular Prevention and Wellness, Houston Methodist, Houston, TX

[3]Division of Epidemiology and Community Health, University of Minnesota, Minneapolis, MN

[4]Department of Radiology, University of Mississippi Medical Center, Jackson, MS

[5]Wake Forest University Population Health Sciences, Winston Salem, NC

[6]Department of Medicine, Lundquist Institute at Harbor-UCLA, Torrance CA

Abstract

Background: Current clinical guidelines recommend a coronary artery calcium (CAC) score of 100 Agatston Units or demographic-specific 75th percentile as high risk thresholds for guiding atherosclerotic cardiovascular disease (ASCVD) preventive therapy. Meanwhile, low CAC can help “de-risk” individuals who may safely defer statin therapy. However, limited data from the early 2000s, including just 208 older Black individuals, inform CAC percentiles for adults age 75–85 and none have been established in adults 85-and-older. This study aims to characterize the distribution of CAC and establish demographic-specific CAC percentiles in the age 75-and-older population.

Methods: We assessed 2,886 participants aged 75-and-older without clinical coronary heart disease (CHD) from the Atherosclerosis Risk in Communities Study visit 7 (2018–2019; n=2,217) and the Multi-Ethnic Study of Atherosclerosis visit 5 (2010–2011; n=669). Prevalence of any CAC >0 and sex- and race-specific CAC percentiles across age were estimated nonparametrically with locally weighted regression models and pooled residual ranking.

Address for Correspondence: Kunihiro Matsushita, MD, PhD, 2024 E. Monument Street, Suite 2-600, Baltimore, Maryland 21287, Telephone: (443) 287-8766, kuni.matsushita@jhu.edu.

The authors declare no conflicting interests.

SUPPLEMENTAL MATERIAL

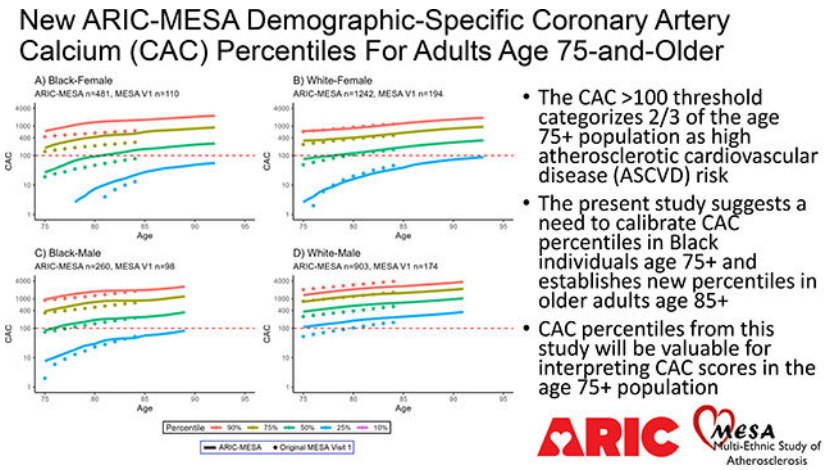
Tables S1–S4

Figures S1–S9

Results: The median age was 80 (interquartile interval: 77–83) years and 60% were female. The prevalence of zero CAC was lowest in White males (4%), followed by Black males (13%), White females (14%), and highest in Black females (18%). Regardless of sex and race, most participants had CAC >100 (62.5%). CAC scores increased with age, with CAC identified in ~95% of participants by age 90-and-older across sex-race subgroups. The 75th percentile corresponded to higher CAC scores for Black older adults (n=741), especially females, than currently used thresholds based on a small sample.

Conclusions: In community-dwelling adults aged 75-and-older free of clinical CHD, the prevalence of zero CAC was 11%, and CAC >100 as a threshold for high ASCVD risk would categorize most of this older population as high risk. Demographic-specific CAC percentiles from this study are a valuable tool for interpreting CAC in the 75-and-older population.

Graphical Abstract:



Keywords

Coronary Artery Calcification; Older Adults; Subclinical Atherosclerosis

Journal Subject Terms:

Epidemiology; Primary Prevention; Computerized Tomography (CT); Imaging; Atherosclerosis; Coronary Artery Disease

Introduction

Coronary artery calcium (CAC) score is a strong predictor of atherosclerotic cardiovascular disease (ASCVD).[1, 2] The 2019 American College of Cardiology/American Heart Association (ACC/AHA) Primary Prevention Guidelines endorsed CAC for refining ASCVD risk stratification among individuals age 40–75 of intermediate risk and guiding primary prevention therapy with statins.[3] The guidelines defined a CAC score of 100 Agatston Units (AU) or age-, sex-, and race-specific 75th percentile as a threshold of high ASCVD risk. Accordingly, CAC is often clinically reported as both an absolute score and a demographic-specific percentile. Current reference percentiles are based on male and female

participants without diabetes at visit 1 of the Multi-Ethnic Study of Atherosclerosis (MESA) in 2000–2002.[4, 5]

There are a few challenges in predicting ASCVD risk in older adults. For example, the relative risks of traditional cardiovascular risk factors with ASCVD become weaker with age.[6, 7] Thus, the prognostic value of these traditional risk factors is limited in older adults. Also, using traditional risk prediction models, almost all older adults are considered at high ASCVD risk based on their age alone.[3] In this context of challenging risk stratification, it has been proposed that CAC may be especially useful in older individuals.[6, 8, 9] However, current CAC percentiles for adults aged 75–84 years are based on data from only 208 Black and 368 White MESA participants. Moreover, current data on demographic-specific CAC percentiles for the growing population of adults 85-and-older are lacking.

Another unique property of CAC is that a zero CAC score (and potentially also CAC 0–9 AU, or <25th percentile) is a powerful *negative* predictor against ASCVD.[3, 10–14] The concept of "de-risking" is particularly relevant in older adults, many of whom receive multiple medications and may be at greater risk of side effects or drug-drug interactions.[3, 15] However, there is a concern that the expected low prevalence of zero or low CAC in the 75-and-older population may limit the ability of CAC to inform shared decision-making conversations involving de-risking older patients.[5, 16] Moving forward, defining contemporary percentiles of CAC scores in the lower end of the spectrum among older populations can provide useful guidance for preventive cardiology decisions in the older adult population.

To fill these important knowledge gaps, using CAC data from 2,217 participants in the Atherosclerosis Risk in Communities (ARIC) study visit 7 (2018–2019) and 669 participants in the most recent MESA visit with CAC information, visit 5 (2010–2011), we aimed to characterize the distribution of CAC and establish percentiles in the 75-and-older population.

Methods

Access to the ARIC and MESA datasets can be requested through the respective coordinating institutions.

Study Population

ARIC recruited 15,792 participants aged 45–64 years in 1987–1989 from four US communities (Forsyth County, North Carolina; Jackson, Mississippi; suburban Minneapolis, Minnesota; and Washington County, Maryland).[17] At ARIC visit 7 (2018–2019), participants without a clinical history of coronary heart disease (CHD) were invited for a non-contrast cardiac-gated computed tomography (CT) to evaluate CAC (n=3,129). Clinical CHD was defined as a medical history or coronary revascularization or myocardial infarction.[18] Among the 2,288 participants who underwent CT, for the present analysis, we excluded participants age <75 years (n=47) and with race other than Black or White (n=7), resulting in a total of 2,234 participants (Figure S1). The exclusion based on race was driven by the very small number of participants from groups other than Black or White. Eligible

participants who did not undergo CT scanning were generally comparable to those who were able to undergo scanning (Table S1).

MESA recruited 6,814 participants free of clinical cardiovascular disease age 45–84 in 2000–2002 from six Communities (Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Northern Manhattan and the Bronx, New York; St. Paul, Minnesota; Forsyth County, North Carolina; and Los Angeles County, California).[19] At MESA visit 5 (2010–2011), which was the most contemporary visit (closest to ARIC visit 7) where CAC scanning was conducted, 3,127 participants without clinical history of myocardial infarction, resuscitated cardiac arrest, or angina underwent CAC scanning. Of these, we excluded participants age <75 years (n=2,128) and with race other than Black or White (n=327) to align with ARIC, resulting in a total of 672 participants (Figure S1).

Demographic and clinical characteristics in the ARIC and MESA samples were largely similar, which made it reasonable to pool the two cohorts in the main analysis (Table S2). After combining the two cohorts and stratifying by sex and race, we further excluded participants at the high-end ages with <5 participants per age year (n=20), to avoid extrapolating volatile percentiles in older age based on a low number of participants. This yielded a final study population of 2,886 participants—2,217 from ARIC and 669 from MESA. Both studies were approved by the respective Institutional Review Boards at each field center and all participants provided informed consent.

CAC Measurement

In both cohorts, non-contrast cardiac-gated CT scans were performed using multidetector CT scanners. Images were acquired by trained technologists and overseen by physicians using identical acquisition protocols. All scans from both studies were interpreted using the same protocol at the CT Reading Center at Harbor-UCLA Medical Center in Los Angeles, California. CAC scores were calculated using the Agatston method and are reported in Agatston Units.[4]

Demographic and Clinical Information

Methods for collecting demographic and clinical information were similar between ARIC and MESA. Participant information was collected at the time of the respective relevant study visit by trained interviewers. Participants were asked to bring all medications to the study visit and trained study personnel coded this information. Age, sex, race, smoking status, and alcohol use were self-reported. Seated blood pressure was measured three times and the average of the last two readings were recorded. Hypertension was defined as systolic blood pressure >140 mmHg, diastolic blood pressure >90 mmHg, or using antihypertensive medications. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Diabetes mellitus was defined as using antidiabetic medications, a self-reported diagnosis of diabetes, fasting glucose ≥7.0 mmol/L, or non-fasting glucose ≥11.1 mmol/L. Standard enzymatic methods were used to measure total cholesterol and high-density lipoprotein cholesterol (HDL-C).[20, 21] Hyperlipidemia was defined as total cholesterol >230 mg/dL, HDL-C< 40 mg/dL for males or <50 mg/dL for females, or treatment with lipid-lowering medications.

Statistical Analysis

All statistical analyses were stratified by sex and race subgroup (Black female, White female, Black male, White male). Participant characteristics were summarized by sex-race groups as medians for continuous variables or counts for categorical variables.

For estimating demographic-specific percentiles of CAC scores, we followed the same non-parametric methods used by McClelland et al. to generate percentiles derived from MESA visit 1 and used in current clinical practice.[3, 5, 22–25] Briefly, we non-parametrically modeled the probability of non-zero CAC score by continuous age using locally-weighted regressions after stratifying participants by sex and race. Since the distributions of CAC were skewed with ~10% of individuals with zero CAC, we first modeled the log-transformed positive (non-zero) portion of the CAC distribution for each sex-race subgroup.[5] Then, we ranked the pooled residuals from the local regression to calculate the j^{th} percentile for j from 1 to 100 of the residuals. The residuals for each percentile were then added back to the age-specific fitted values and then exponentiated to yield CAC corresponding to each j^{th} percentile in the non-zero portion of the distribution over age, CAC_j. To estimate percentiles for the overall CAC distribution, we converted CAC_j for the j^{th} percentile, into the percentile for the overall distribution including participants with zero CAC using $100 * (p + [(1 - p) * j] / 100)$ where p is the proportion of individuals with zero CAC within the given age, sex, and race.

To evaluate whether any calibration of CAC percentiles may be needed in clinical practice, we compared the percentiles from the current study with a larger sample size versus that based on the limited sample size from MESA visit 1.[5] Additionally, though less precise than the modeled CAC percentiles, we also calculated empirical CAC percentiles as a supplementary analysis. We also repeated all analyses in ARIC and MESA separately to assess potential differences in CAC distribution within the two cohorts. Sensitivity analyses were also conducted after excluding individuals with diabetes, as was done for the MESA visit 1 percentiles, and stratifying by statin use. To evaluate whether there was evidence of a potential health survivor effect with age, we used MESA data (since CAC data on adults age<75 was limited in ARIC) to re-estimate CAC percentiles including participants age <75, an additional n=1,394 participants with ages ranging from 54–74. We also characterized the association between traditional cardiovascular risk factors (hypertension, smoking, diabetes, and hyperlipidemia) and CAC percentiles, using multivariable linear regression adjusting for all other listed risk factors.

All analyses were performed using R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study Participants

The median age of the 2,886 participants was 80 years (interquartile interval [IQI]: 77 to 83), with 60% female and 26% Black individuals. In these 75-and-older participants, there was a 77% prevalence of hypertension, 27% prevalence of diabetes, 50% used statins, and 4% were current smokers. Black participants tended to have a higher prevalence of hypertension and diabetes, while White participants were more often current alcohol

users (Table 1). In females, Black participants tended to have a higher BMI than White participants, while BMI was similar between Black and White males. Females tended to have higher systolic blood pressure and total cholesterol, while males were more likely to have diabetes and be on statin medication. The age distribution of participants by sex-race group is depicted in Figure S2.

Absolute CAC Scores

The most prevalent CAC category was 100–399 (24.5%), and most participants had CAC >100 (62.5%; Table 2). Only 18.1% of White males had CAC <100. The overall prevalence of zero CAC was 11.4%, and the prevalence of zero CAC was lowest in White males (4%), followed by Black males (13%), White females (14%), and highest in Black females (18%). Across all sex-race groups, prevalence of any CAC (i.e., CAC >0) increased with age (Figure 1), and by age 90, the prevalence of any CAC was over 95% across all sex-race groups. Black males demonstrated less prevalent CAC than White males at any given age, whereas the prevalence in Black females exceeded that of White females around age of 85. Results were largely comparable when the ARIC and MESA subsamples were evaluated separately (Figure S3).

CAC Percentiles

The CAC score corresponding to a given percentile tended to increase with age across sex-race categories and was highest in White males (Figure 2). The CAC score corresponding to the 75th percentile exceeded 1,000 in White males across most age ranges above 75 years (gold line in Figure 2D) but mostly resided within the range of 180 to 1,000 in the other three race-sex categories (gold line in Figure 2A–C). The respective 75th percentile CAC scores at ages 75 and 85 were 180 and 636 in Black females, 320 and 592 in White females, 373 and 874 in Black males, and 789 and 1,575 in White males

Regardless of sex and race, the 50th percentile (green line in Figure 2) crossed over the CAC >100 threshold for most participants of ages 75-and-older. CAC scores corresponding to the 25th percentile (blue line in Figure 2) remained below 100 for all race-sex categories, except for White males where the 25th percentile was consistently greater than CAC 100. The CAC score corresponding to the 10th percentile (purple line in Figure 2) ranged from 19 to 101 in White males but was <17 in the other three race-sex categories. Figure S4 shows the same data with the Y-axis on an arithmetic scale.

Empirical percentiles generally aligned with regression-based percentiles, as shown in Table S3 and Figure S5. When stratifying by study cohort, largely consistent results were observed between ARIC and MESA (Figure S6). Results were also similar after excluding individuals with diabetes (Figure S7). In subgroup analyses, stratifying by statin use yielded modestly higher CAC scores at a given percentile in statin users compared to non-users (Figure S8). Expanding the age range criteria to include participants age<75 in the MESA cohort, because CAC data on younger participants from ARIC was limited, there was no evident change in CAC percentile trajectory from mid-to-late life, except in White-Males where CAC burden seems to plateau at age 80+ (Figure S9). Hypertension, smoking, diabetes, and hyperlipidemia were all significantly associated with higher CAC percentiles (Table S4).

Contemporary ARIC-MESA CAC Percentiles vs. MESA 2000–2002 Percentiles

For White females, the CAC percentiles derived from the smaller 2000–2002 MESA visit 1 sample were very similar to current ARIC-MESA percentiles (Figure 3B). [5] In White males, the 75th percentile was almost identical between MESA visit 1 and the current ARIC-MESA dataset (Figure 3D). However, the 90th percentile corresponded to a lower CAC score in the present combined ARIC-MESA dataset than in MESA visit 1, while 50th and 25th percentiles showed higher CAC scores. In Black participants, the CAC score at a given percentile was consistently greater in the current ARIC-MESA dataset than in MESA visit 1, particularly in female participants (Figure 3A–B). For example, the 75th percentile for Black females age 75 years was 180 in ARIC-MESA versus 138 in MESA visit 1.

When we compared data from MESA visit 5 and MESA visit 1, CAC scores corresponding to the percentiles were generally similar in Black males, but we observed some differences for the other three race-sex categories (Figure S10).

Discussion

In contemporary community-dwelling adults age 75-and-older, the prevalence of zero CAC was 11%, ranging from 4% to 18% across sex-race subgroups. CAC burden was greatest in White males, followed by Black males, White females, and was lowest in Black females. Most of our study sample (62.5%) had CAC >100, which also means that over 1/3 of these older adults age 75-and-older had CAC scores below 100, an important finding as most of these individuals would be uniformly considered at high ASCVD risk using traditional risk scores because of their advanced age. CAC scores for a given percentile tended to increase with age. By age 90, ~95% of participants had some CAC, regardless of sex and race. At the 75th percentile, CAC exceeded 1,000 at all ages above 75 for White males and resided in the range of 180 to 1,000 in the other race-sex groups. For the 25th percentile, CAC remained below 100 for all sex-race categories, except for White males where it was consistently greater than CAC 100. This study describes contemporary CAC percentile scores in the age 75-and-older US population and has important implications for the preventive care of this growing patient population, the management of which is often complex.

CAC data in community-dwelling older adults age 75-and-older are surprisingly sparse. For example, CAC percentiles for clinical decision-making in the ACC/AHA primary prevention guidelines are based on data from MESA visit 1 (2000–2002)[3, 5], which included only 208 Black and 368 White participants aged 75–84 and did not have any data in older adults age 85-and-older.[3, 4]. The contemporary CAC percentiles reported in this study build upon MESA visit 1-derived percentiles and present older adult percentiles in a more geographically diverse population from a larger dataset pooling two cohorts. These age 75-and-older CAC percentiles will be valuable for physician-patient communication and can be beneficial for identifying highest risk older adults to target primary prevention therapies. This is especially relevant for the older adult population, since a high CAC threshold of 100 may not be helpful for risk discrimination because most older adults have CAC greater than this threshold.

The determination of optimal thresholds of CAC score in the 75-and-older population (especially >85 years old) requires a broad range of evidence, including descriptive studies of population distribution like the present study, prospective studies with clinical outcomes, available treatment options (e.g., statins) and their cost-effectiveness. Prior studies have suggested that CAC is highly predictive of CHD in older adults.[10, 13, 26–28] However, whether CAC evaluation can provide net value in guiding medical management in oldest individuals is under study. The ongoing NIH-funded PREVENTABLE trial will evaluate these two important questions: 1) the efficacy and safety of statin therapy in age 75-and-older adults overall, and 2) the potential role of baseline CAC scores in this context. As the older adult population continues to expand worldwide, in the coming decades we expect demographic-specific CAC percentiles derived in the present work to become very useful for contextualizing the interpretation of CAC scores in the older age strata, both clinically and for future research studies.

The higher CAC scores corresponding to a given percentile among Black individuals in the present study, compared to MESA visit 1, deserves discussion. Since most Black older adults in the present study were from Jackson, Mississippi (59% of Black participants in the entire study and 91% of ARIC Black participants), these differences in CAC percentiles may reflect geographic and demographic differences within Black populations. Also, a larger sample size in the current analysis compared to MESA visit 1 is noteworthy (481 versus 110 Black female and 260 versus 98 Black male). Thus, for Black adults age 75-and-older, clinicians should consider referring to CAC scores corresponding to the 75th percentile from this study, rather than from MESA visit 1.

In contrast to CAC percentiles for Black individuals, our data suggests that there is no need to revise CAC percentiles for White females. For White males, CAC score corresponding to the 75th percentile, a threshold of high CAC, in White older males was almost identical between our study and the original MESA visit 1. However, the interpretation of CAC scores corresponding to percentiles greater or smaller than 75th would need some calibration. For example, for an 80-year-old White male, a CAC of 2000 would place him at an 83th percentile according to MESA visit 1 data, but he would now be at the 90th percentile. On the other hand, an 80-year-old White male with CAC 400 would move down from a MESA visit 1 50th percentile to a 39th percentile from our updated study.

In addition to characterizing ASCVD high-risk in the 75-and-older population, zero and low CAC can identify lower risk older adults that might safely avoid preventive cardiac pharmacotherapies.[16, 29] Our study, with an 11% prevalence of zero CAC, indicates a number needed to scan of 9 in the age-75-and-older population to identify an older adult with low ASCVD risk. However, in the White male population where the prevalence of zero CAC was only 4% and by age 90-and-older for all other race-sex groups, zero CAC was rare, suggesting a need to explore another threshold beyond zero CAC (e.g., CAC <10 or <25th percentile) for identifying low ASCVD risk in these populations.[30, 31] Although ultimately survival analyses are necessary to address this issue, the CAC percentiles in the present study will provide a foundation for contextualizing low CAC in older adults.

Study Limitations

CAC percentiles in this study are only established in Black and White older adults since data from other racial and ethnic groups are limited in the primary dataset of our study from ARIC. Second, as noted above, most Black individuals enrolled in ARIC were from Jackson, Mississippi. Thus, although this is the largest and most geographically diverse study to date on CAC in community-dwelling older adults age 75-and-older, studies of Black individuals from other geographic areas in the United States may help confirm our estimates. Also, additional studies are important to validate the 10^{th} and 90^{th} percentiles, especially in older Black participants, since the sample size to estimate these tail-end percentiles can be limited. Moreover, future studies are required to further quantify the associations of CAC percentiles and score with cardiovascular outcomes in the 75-and-older populations. Lastly, our study included participants who were able to attend the study visit and undergo CT scanning and, thus, are likely to be healthier than the entire target population of older adults. However, participants of ARIC visit 7 and MESA visit 5 have long-established bond with these study cohorts over decades. Therefore, they likely have higher participation rates and more closely represent the overall older adult population than any cohorts newly recruiting older adults age 75-and-older. Additionally, this study population likely reflects the real-world older adult population that can attend a clinic visit and attain CAC scanning which these percentiles are relevant to.

Conclusions

In this large, pooled cohort of community-dwelling Black and White adults aged 75-and-older free of clinical CHD, we established demographic-specific CAC percentiles and characterized the distribution of CAC. The prevalence of zero CAC was 11%, and CAC >100 as a threshold for high ASCVD risk would categorize almost 2/3 of this older population as high ASCVD risk. Thus, these demographic-specific CAC percentiles can be a valuable tool for contextualizing the interpretation of CAC scores in the 75-and-older population. This is especially the case for Black individuals, who comprised a small number of participants in the original data used to derive current clinical reference percentiles.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

The authors thank the staff and participants of the ARIC and MESA study for their important contributions.

SOURCES OF FUNDING

The ARIC study has been funded in whole or in part with federal funds from the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), Department of Health and Human Services, under contract numbers HHSN268201700001I, HHSN268201700002I, HHSN268201700003I, HHSN268201700005I, and HHSN268201700004I. CT scans to evaluate CAC in ARIC were supported by R01HL136592 (Co-PIs: Drs. Matsushita and Blaha). The MESA was supported by contracts N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, and N01-HC-9516 from the NHLBI and by grants UL1-RR-024156 and UL1-RR-025005 from National Center for Research Resources. F.W. received support from the NIH T32 institutional training grant (T32 HL007024).

Non-standard Abbreviations and Acronyms

AU	Agatston Units
ACC/AHA	American College of Cardiology/American Heart Association
ARIC	Atherosclerosis Risk in Communities
ASCVD	Atherosclerotic cardiovascular disease
BMI	Body mass index
CT	Computed tomography
CAC	Coronary artery calcium
CHD	Coronary heart disease
HDL-C	High-density lipoprotein cholesterol
IQI	Interquartile interval
MESA	Multi-Ethnic Study of Atherosclerosis

REFERENCES

1. Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, Liu K, Shea S, Szklo M, Bluemke DA, O'Leary DH, Tracy R, Watson K, Wong ND and Kronmal RA. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. N Engl J Med. 2008;358:1336–45. [PubMed: 18367736]
2. Erbel R, Mohlenkamp S, Moebus S, Schmermund A, Lehmann N, Stang A, Dragano N, Gronemeyer D, Seibel R, Kalsch H, Brocker-Preuss M, Mann K, Siegrist J, Jockel KH and Heinz Nixdorf Recall Study Investigative G. Coronary risk stratification, discrimination, and reclassification improvement based on quantification of subclinical coronary atherosclerosis: the Heinz Nixdorf Recall study. J Am Coll Cardiol. 2010;56:1397–406. [PubMed: 20946997]
3. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC, Virani SS, Williams KA, Yeboah J and Ziaeian B. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;140:e596–e646. [PubMed: 30879355]
4. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M and Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol. 1990;15:827–32. [PubMed: 2407762]
5. McClelland RL, Chung H, Detrano R, Post W and Kronmal RA. Distribution of coronary artery calcium by race, gender, and age: results from the Multi-Ethnic Study of Atherosclerosis (MESA). Circulation. 2006;113:30–7. [PubMed: 16365194]
6. Lind L, Sundström J, Ärnlöv J and Lampa E. Impact of Aging on the Strength of Cardiovascular Risk Factors: A Longitudinal Study Over 40 Years. J Am Heart Assoc. 2018;7: e007061. [PubMed: 29306895]
7. Abbott RD, Curb JD, Rodriguez BL, Masaki KH, Yano K, Schatz IJ, Ross GW and Petrovitch H. Age-related changes in risk factor effects on the incidence of coronary heart disease. Ann Epidemiol. 2002;12:173–81. [PubMed: 11897175]
8. Psaty BM, Furberg CD, Kuller LH, Bild DE, Rautaharju PM, Polak JF, Bovill E and Gottdiener JS. Traditional risk factors and subclinical disease measures as predictors of first myocardial infarction

in older adults: the Cardiovascular Health Study. Arch Intern Med. 1999;159:1339–47. [PubMed: 10386510]

9. Mukamal KJ, Kronmal RA, Tracy RP, Cushman M and Siscovick DS. Traditional and novel risk factors in older adults: cardiovascular risk assessment late in life. Am J Geriatr Cardiol. 2004;13:69–80. [PubMed: 15010653]
10. Tota-Maharaj R, Blaha MJ, McEvoy JW, Blumenthal RS, Muse ED, Budoff MJ, Shaw LJ, Berman DS, Rana JS, Rumberger J, Callister T, Rivera J, Agatston A and Nasir K. Coronary artery calcium for the prediction of mortality in young adults <45 years old and elderly adults >75 years old. Eur Heart J. 2012;33:2955–62. [PubMed: 22843447]
11. Valenti V, Ó Hartaigh B, Heo R, Cho I, Schulman-Marcus J, Gransar H, Truong QA, Shaw LJ, Knapper J, Kelkar AA, Sandesara P, Lin FY, Sciarretta S, Chang HJ, Callister TQ and Min JK. A 15-Year Warranty Period for Asymptomatic Individuals Without Coronary Artery Calcium: A Prospective Follow-Up of 9,715 Individuals. JACC Cardiovasc Imaging. 2015;8:900–9. [PubMed: 26189116]
12. Blaha MJ, Cainzos-Achirica M, Greenland P, McEvoy JW, Blankstein R, Budoff MJ, Dardari Z, Sibley CT, Burke GL, Kronmal RA, Szklo M, Blumenthal RS and Nasir K. Role of Coronary Artery Calcium Score of Zero and Other Negative Risk Markers for Cardiovascular Disease: The Multi-Ethnic Study of Atherosclerosis (MESA). Circulation. 2016;133:849–58. [PubMed: 26801055]
13. Wang FM, Rozanski A, Arnson Y, Budoff MJ, Miedema MD, Nasir K, Shaw LJ, Rumberger JA, Blumenthal RS, Matsushita K, Blaha MJ and Berman DS. Cardiovascular and All-Cause Mortality Risk by Coronary Artery Calcium Scores and Percentiles Among Older Adult Males and Females. Am J Med. 2021;134:341–350. [PubMed: 32822664]
14. Mortensen MB, Fuster V, Muntendam P, Mehran R, Baber U, Sartori S and Falk E. Negative Risk Markers for Cardiovascular Events in the Elderly. J Am Coll Cardiol. 2019;74:1–11. [PubMed: 31272534]
15. Hoel RW, Giddings Connolly RM and Takahashi PY. Polypharmacy Management in Older Patients. Mayo Clin Proc. 2021;96:242–256. [PubMed: 33413822]
16. Newman AB, Naydeck BL, Sutton-Tyrrell K, Feldman A, Edmundowicz D and Kuller LH. Coronary artery calcification in older adults to age 99: prevalence and risk factors. Circulation. 2001;104:2679–84. [PubMed: 11723018]
17. The ARIC investigators. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. Am J Epidemiol. 1989;129:687–702. [PubMed: 2646917]
18. White AD, Folsom AR, Chambless LE, Sharret AR, Yang K, Conwill D, Higgins M, Williams OD and Tyroler HA. Community surveillance of coronary heart disease in the Atherosclerosis Risk in Communities (ARIC) Study: methods and initial two years' experience. J Clin Epidemiol. 1996;49:223–33. [PubMed: 8606324]
19. Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, Greenland P, Jacob DR Jr., Kronmal R, Liu K, Nelson JC, O'Leary D, Saad MF, Shea S, Szklo M and Tracy Multi-Ethnic Study of Atherosclerosis: objectives and design. Am J Epidemiol. 2002;156:871–81. [PubMed: 12397006]
20. Papp AC, Hatzakis H, Bracey A and Wu KK. ARIC hemostasis study--I. Development of a blood collection and processing system suitable for multicenter hemostatic studies. Thromb Haemost. 1989;61:15–9. [PubMed: 2526384]
21. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002;106:3143–421. [PubMed: 12485966]
22. O'Brien PC and Dyck PJ. Procedures for setting normal values. Neurology. 1995;45:17–23. [PubMed: 7824110]
23. Hecht H, Blaha MJ, Berman DS, Nasir K, Budoff M, Leipsic J, Blankstein R, Narula J, Rumberger J and Shaw LJ. Clinical indications for coronary artery calcium scoring in asymptomatic patients: Expert consensus statement from the Society of Cardiovascular Computed Tomography. J Cardiovasc Comput Tomogr. 2017;11:157–168. [PubMed: 28283309]

24. Orringer CE, Blaha MJ, Blankstein R, Budoff MJ, Goldberg RB, Gill EA, Maki KC, Mehta L and Jacobson TA. The National Lipid Association scientific statement on coronary artery calcium scoring to guide preventive strategies for ASCVD risk reduction. J Clin Lipidol. 2021;15:33–60. [PubMed: 33419719]
25. Javaid A, Dardari ZA, Mitchell JD, Whelton SP, Dzaye O, Lima JAC, Lloyd-Jones DM, Budoff M, Nasir K, Berman DS, Rumberger J, Miedema MD, Villines TC and Blaha MJ. Distribution of Coronary Artery Calcium by Age, Sex, and Race Among Patients 30–45 Years Old. Journal of the American College of Cardiology. 2022;79:1873–1886. [PubMed: 35550683]
26. Yano Y, O'Donnell CJ, Kuller L, Kavousi M, Erbel R, Ning H, D'Agostino R, Newman AB, Nasir K, Hofman A, Lehmann N, Dhana K, Blankstein R, Hoffmann U, Möhlenkamp S, Massaro JM, Mahabadi AA, Lima JAC, Ikram MA, Jöckel KH, Franco OH, Liu K, Lloyd-Jones D and Greenland P. Association of Coronary Artery Calcium Score vs Age With Cardiovascular Risk in Older Adults: An Analysis of Pooled Population-Based Studies. JAMA Cardiol. 2017;2:986–994. [PubMed: 28746709]
27. Tota-Maharaj R, Blaha MJ, Blankstein R, Silverman MG, Eng J, Shaw LJ, Blumenthal RS, Budoff MJ and Nasir K. Association of Coronary Artery Calcium and Coronary Heart Disease Events in Young and Elderly Participants in the Multi-Ethnic Study of Atherosclerosis: A Secondary Analysis of a Prospective, Population-Based Cohort. Mayo Clinic Proceedings. 2014;89:1350–1359. [PubMed: 25236430]
28. Mortensen MB, Fuster V, Muntendam P, Mehran R, Baber U, Sartori S and Falk E. A Simple Disease-Guided Approach to Personalize ACC/AHA-Recommended Statin Allocation in Elderly People: The BioImage Study. J Am Coll Cardiol. 2016;68:881–91. [PubMed: 27561760]
29. Blaha MJ, Blankstein R and Nasir K. Coronary Artery Calcium Scores of Zero and Establishing the Concept of Negative Risk Factors. J Am Coll Cardiol. 2019;74:12–14. [PubMed: 31272536]
30. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, Braun LT, de Ferranti S, Faiella-Tommasino J, Forman DE, Goldberg R, Heidenreich PA, Hlatky MA, Jones DW, Lloyd-Jones D, Lopez-Pajares N, Ndumele CE, Orringer CE, Peralta CA, Saseen JJ, Smith SC, Sperling L, Virani SS and Yeboah J 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;139:e1082–e1143. [PubMed: 30586774]
31. Hecht HS, Cronin P, Blaha MJ, Budoff MJ, Kazerooni EA, Narula J, Yankelevitz D and Abbara S. 2016 SCCT/STR guidelines for coronary artery calcium scoring of noncontrast noncardiac chest CT scans: A report of the Society of Cardiovascular Computed Tomography and Society of Thoracic Radiology. J Thorac Imaging. 2017;32:W54–W66. [PubMed: 28832417]

CLINICAL PERSPECTIVE

In a large, pooled cohort of community-dwelling Black and White adults age 75-and-older free of clinical CHD, we established demographic-specific CAC percentiles. The prevalence of zero CAC was 11%, and 2/3 of adults 75-and-older had CAC >100, a threshold for high ASCVD risk, suggesting the value of the other high CAC threshold of demographic-specific 75th percentile in this population. The distribution of CAC was highest in White males, followed by Black males, White females, and lowest in Black females. The demographic-specific CAC percentiles for the 75-and-older population established in this study are a valuable tool for interpreting CAC and have important implications for guiding preventive therapy in this growing patient population.

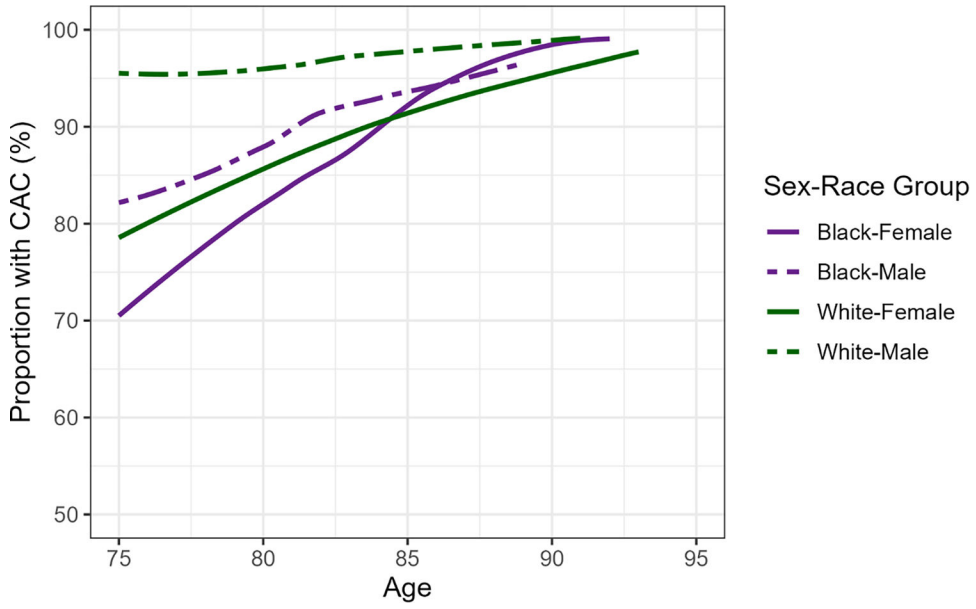


Figure 1.
Demographic-specific prevalence of coronary artery calcium (CAC) across age.

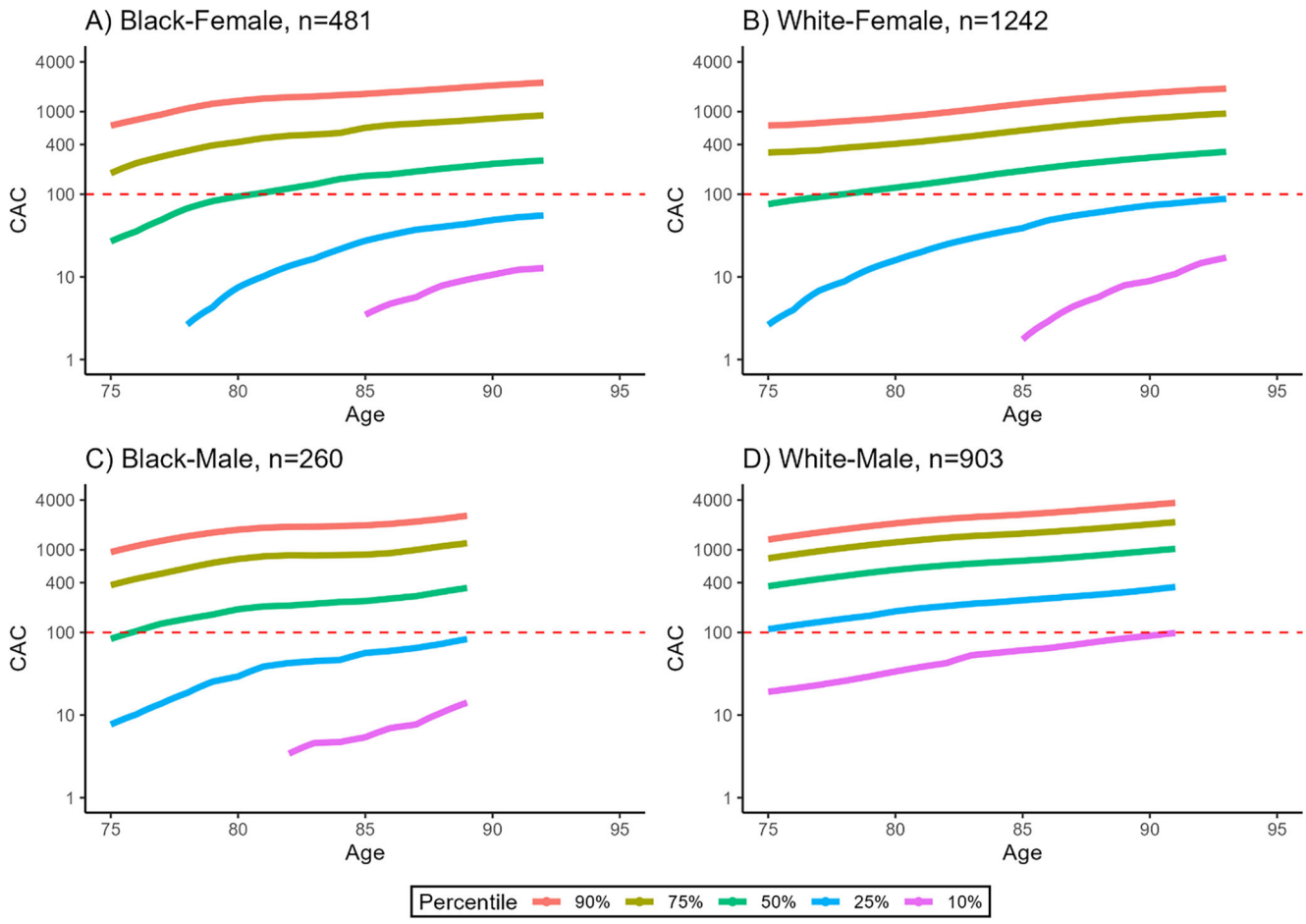


Figure 2.

Estimated demographic-specific ARIC-MESA percentiles for coronary artery calcium (CAC) across age by sex-race groups. A) Black-Female; B) White-Female; C) Black-Male; D) White-Male.

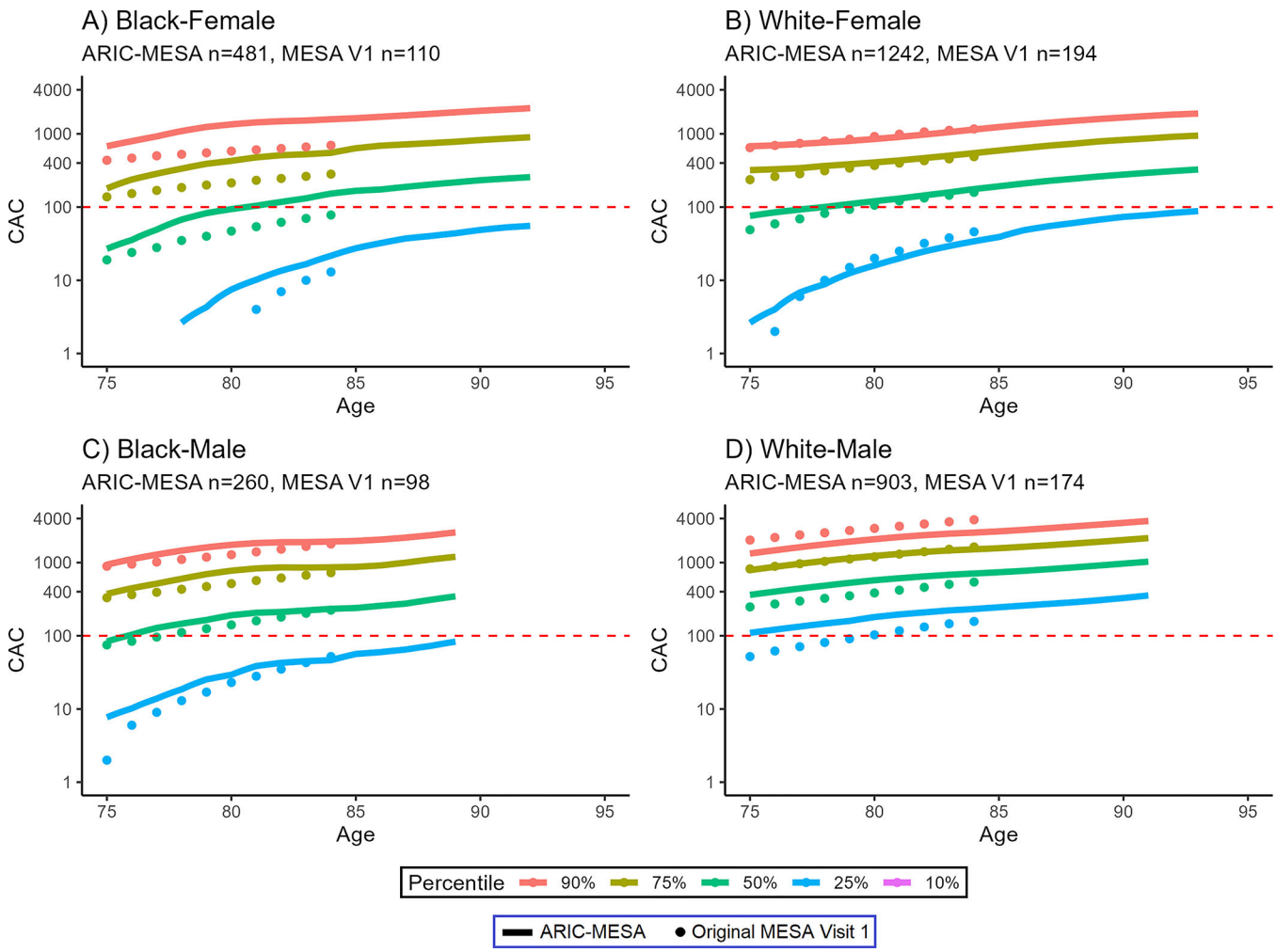


Figure 3.

Comparison of original MESA Visit 1 percentiles and ARIC-MESA percentiles by sex-race groups. A) Black-Female; B) White-Female; C) Black-Male; D) White-Male.

Table 1.

Participant characteristics at the time of coronary artery calcium (CAC) scan.

	Overall	Female		Male	
		Black	White	Black	White
Sample Size (n)	2886	481	1242	260	903
Age, years (median [IQI])	80 [77, 83]	79 [77, 83]	80 [77, 83]	79 [76, 82]	80 [77, 83]
BMI, kg/m^2 (median [IQI])	27.4 [24.4, 30.8]	29.2 [25.8, 34.2]	26.4 [23.4, 29.9]	27.7 [25.0, 30.7]	27.7 [24.9, 30.7]
Current Smoker (%)	127 (4.4)	24 (5.0)	52 (4.2)	19 (7.4)	32 (3.6)
Current Alcohol User (%)	1460 (50.7)	103 (21.5)	692 (55.9)	95 (36.7)	570 (63.3)
SBP, mmHg (median [IQI])	132 [120, 145]	133 [121, 148]	135 [122, 148]	130 [118, 145]	129 [117, 141]
DBP, mmHg (median [IQI])	66 [59, 73]	65 [59, 72]	66 [59, 73]	67 [61, 75]	67 [60, 73]
Hypertension (%)	2190 (76.6)	430 (89.4)	910 (74.2)	214 (82.9)	636 (71.1)
Hypertension medication use (%)	2130 (73.9)	430 (89.4)	852 (68.6)	200 (77.2)	648 (72.0)
Diabetes (%)	778 (27.0)	168 (35.1)	275 (22.2)	101 (39.0)	234 (25.9)
Cholesterol, mg/dL (median [IQI])	177 [152, 204]	187 [162, 212]	187 [162, 215]	167 [141, 197]	160 [139, 186]
HDL-C, mg/dL (median [IQI])	51 [42, 62]	57 [48, 68]	54 [46, 65]	49 [42, 58]	44 [38, 53]
Statin use (%)	1367 (47.9)	213 (44.7)	554 (45.2)	123 (48.2)	477 (53.5)

Values are median [IQI], or counts (%) as noted.

BMI = body mass index, DBP = diastolic blood pressure, HDL-C = high-density lipoprotein cholesterol, IQI = interquartile interval, SBP = systolic blood pressure

Table 2.

Distribution of absolute coronary artery calcium (CAC) score categories overall and by sex-race groups.

CAC Score Categories	Overall	Female		Male	
		Black	White	Black	White
0	328 (11.4)	86 (17.9)	176 (14.2)	33 (12.7)	33 (3.7)
1–9	178 (6.2)	44 (9.1)	97 (7.8)	17 (6.5)	20 (2.2)
10–99	576 (20.0)	118 (24.5)	288 (23.2)	60 (23.1)	110 (12.2)
100–399	707 (24.5)	107 (22.2)	338 (27.2)	61 (23.5)	201 (22.3)
400–999	591 (20.5)	64 (13.3)	229 (18.4)	49 (18.8)	249 (27.6)
≥1000	506 (17.5)	62 (12.9)	114 (9.2)	40 (15.4)	290 (32.1)

Values are counts (%). CAC = coronary artery calcium