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# Cardiovascular Disease Risk Scores' Relationship to Subclinical Cardiovascular Disease Among HIV-Infected and –Uninfected Men

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## Abstract

**Objective**—To study cardiovascular disease risk score utility we 1) compared the association between Framingham Risk Score (FRS)/pooled cohort equation (PCE) categories and coronary artery plaque presence by HIV serostatus and 2) evaluated whether D:A:D risk category more accurately identifies plaque in HIV-infected men.

**Design**—Cross-sectional analysis within a substudy of the Multicenter AIDS Cohort Study.

**Methods**—Cardiac CT was performed to assess coronary plaque. We evaluated the association of plaque with increasing CVD risk score category, stratified by HIV serostatus, using logistic regression. ROC curves compared the discrimination of the scores for plaque by HIV serostatus. The sensitivity and specificity of the risk scores were compared in HIV-infected men.

**Results**—The risk score category—plaque associations were stronger among HIV-uninfected men than HIV-infected men, except for non-calcified plaque. For example, the odds of coronary artery calcium (CAC)>0 were 7.03 (95% CI 4.21, 11.76) times greater among men in the PCE high risk versus low risk category among HIV-uninfected men, compared to just 3.13 (95% CI 2.13, 4.61) times greater among men in the high risk versus low risk category among HIV-infected men. Among HIV-infected men, high risk category by PCE identified the greatest percent of men with plaque/stenosis, but with lower specificity than D:A:D and FRS. The prevalence of CAC>0 among men in the PCE low risk category was 26.5% (HIV-uninfected men) and 36.0% (HIV-infected men).

**Conclusions**—FRS and PCE categories associate with plaque burden better in HIV-uninfected men. No risk score delivered both high sensitivity and specificity among HIV-infected men.

## Keywords

cardiovascular disease; risk scores; HIV; cardiac CT; subclinical atherosclerosis

## Introduction

Among HIV-infected individuals, CVD-related mortality is an important cause of death [1, 2] and epidemiologic studies have shown a greater prevalence of subclinical coronary atherosclerosis among HIV-infected compared to HIV-uninfected individuals [3–5]. Accurate CVD risk prediction, therefore, is essential for optimal long-term management of HIV-infected persons. CVD risk scores, including the Framingham Risk Score (FRS) and the American College of Cardiology/American Heart Association (ACC/AHA) PCE [6, 7], predict risk for CVD events and are recommended for use in clinical settings to determine need for preventive therapies, such as lipid-lowering medications. HIV-infected patients have higher FRS than age- and sex- matched HIV-uninfected controls due to more smoking and low HDL cholesterol levels [8]. However, FRS has been shown to underestimate cardiac events among HIV-infected persons as their duration of antiretroviral therapy (ART) increased [9]. A low level of agreement between FRS and subclinical atherosclerosis, as measured by carotid intima media thickness, has been demonstrated among HIV-infected persons, with a large proportion (56.4%) of persons with subclinical atherosclerosis classified as low risk by FRS [10]. This may reflect HIV-related immune activation despite suppressed HIV viremia [11].

Investigators from the Data Collection on Adverse Effects of Anti-HIV Drugs (D:A:D) group developed an enhanced risk equation that includes HIV-specific factors for use among HIV-infected individuals [12]. The D:A:D score performed better than the FRS in predicting subclinical atherosclerosis measured by intimal-media thickness (IMT) among HIV-infected men; however, about 17% of HIV-infected patients characterized as low risk by both equations had evidence of atherosclerosis as assessed by IMT[13]. Compared with carotid IMT, presence of CAC has been shown to improve prediction of incident CVD in the general population [14]. Currently, there is limited data on the associations between cardiovascular disease risk score and subclinical atherosclerosis (including CAC) among individuals with

HIV. One study reported a higher FRS among HIV-infected individuals with versus without CAC (mean FRS of 0.19 and 0.12, respectively) [15].

Our primary objective was to examine the associations of two general population CVD risk scores (the FRS and the ACC/AHA PCE) with the presence of coronary artery plaque among well-characterized HIV-infected and similar at-risk HIV-uninfected men, and whether these associations differ by HIV serostatus.

## Methods

### Study Population

The MACS was initiated in 1984 as a study of men who have sex with men conducted at four study sites in Baltimore/Washington, DC, Chicago, Los Angeles, and Pittsburgh. A total of 6,972 men have been enrolled over three time periods (1984–85, 1987–90, and 2001–03) and enrollment is currently open. Details of the study design and methods have been published [16].

### Selection Criteria

This analysis included data from a nested CVD CT scan study, which enrolled 1001 MACS participants who were 40–70 years of age, weighed less than 300 pounds, and had no history of coronary artery revascularization [4]. Only 2% of the sample were missing data on at least one variable required to generate the three risk scores; these participants were excluded from the analytic sample. We also excluded 10 men with adjudicated cardiovascular events (myocardial infarction, stroke, transient ischemic attack, peripheral arterial disease, or nonfatal cardiac arrest) prior to their plaque measurement. The protocol was approved by Institutional Review Boards at each site and each study participant signed informed consents.

### Plaque Outcomes

The details of the CT scanning have been published previously [4, 17]. Briefly, non-contrast cardiac CT scans for coronary artery calcium (CAC) and coronary CT angiography (CTA) for other plaque outcomes were performed between January 2010 and August 2013. Men with atrial fibrillation, chronic kidney disease [estimated glomerular filtration rate (GFR) $<60$ ml/min/m$^2$ during a prior MACS study visit] or a history of IV contrast allergy were excluded from CTA studies, and GFR$>60$ ml/min/m$^2$ was verified within one month for those men undergoing CTA. Images from the scans were evaluated at a core CT reading center (Los Angeles Biomedical Research Institute at Harbor-UCLA) by trained, experienced readers who were blinded to participant characteristics including HIV serostatus. CAC scores were calculated using the Agatston method. For the CTA studies, each segment was analyzed using the modified 15-segment model of the American Heart Association [18].

Each coronary segment was classified as normal or containing non-calcified plaque, mixed plaque (<50% of plaque area occupied by calcium) or calcified plaque (definitions provided in previous manuscript) and/or stenosis 50% [4, 17]. The outcomes for this analysis

included the presence of plaque (CAC>0 on non-contrast CT, and any coronary plaque, non-calcified plaque or mixed plaque on CTA), and coronary artery stenosis    50%.

### Risk Score Calculation

For each participant, we calculated the following cardiovascular disease risk scores: the Framingham hard coronary heart disease (CHD) Risk Score using code based on the FRS score sheets in the Adult Treatment Panel III (http://www.nhlbi.nih.gov/files/docs/guidelines/atglance.pdf) [6] the ACC/AHA PCE [7], and for HIV-infected participants, the D:A:D Score [12]. The participant characteristics that are included in the calculation of each risk score, the risk time horizon, and the outcome(s) predicted by each score are listed (see Table, Supplemental Digital Content 1, which shows each risk score). Score calculation is described in detail (see Text file, Supplemental Digital Content 2, describing the variables that are included in the risk score).

For the FRS, individuals with >20% estimated risk of MI and coronary death within 10 years are categorized as high risk; persons with 10–20% risk are moderate risk, and persons with <10% risk are low risk. All diabetic participants were classified as FRS high risk *a priori*, regardless of FRS score. The PCE classifies as high risk, individuals with    7.5% risk of coronary death or nonfatal MI, or fatal or nonfatal stroke within 10 years; moderate risk for those with 5–7.5% risk, and low risk for those with <5% risk. The D:A:D score classifies individuals with >10% risk of nonfatal and fatal MI within 5 years as very high risk, 5–10% as high risk, 1–5% as moderate risk, and <1% as low risk. We combined the D:A:D very high and high risk categories. Our aim was to compare the extent to which the risk categories used clinically as specified by the various risk algorithms are associated with contemporaneous subclinical coronary disease, therefore, risk categories, rather than risk scores, were our primary predictors.

### Statistical Analysis

Distributions of demographic, behavioral, and clinical characteristics of HIV-infected and uninfected men were compared using the chi-square or Wilcoxon rank sum tests for categorical and continuous variables, respectively.

For each plaque outcome, we fit a logistic regression model using predictors of risk score category and HIV serostatus. Interaction terms were included to evaluate whether the association between risk score category and plaque differed by HIV serostatus. Separate models were run for each general risk score equation (PCE and FRS). Discrimination, the ability of the risk score to classify participants with and without plaque, was assessed separately among HIV-infected and HIV-uninfected men based on the receiver operating characteristic (ROC) curve. The area under the ROC curve was calculated using the trapezoidal rule and was compared by HIV status using a test for two independent samples.

We evaluated the discrimination of the D:A:D score compared to the FRS and PCE among HIV-infected men, using sensitivity and specificity of the risk category cutpoints in addition to the global area under the ROC curve metric. We evaluated the sensitivity and specificity at two thresholds: 1) greater than or equal to the high risk category, and alternatively 2) greater than or equal to the moderate risk categories, for each of the three scores. Sensitivity was the

probability of being classified as ≥ high risk (alternatively ≥ moderate risk) risk among men with atherosclerosis. Specificity was the probability of being classified as < high risk (alternatively < moderate risk) risk among men without atherosclerosis. We compared the sensitivity and specificity of the algorithms using McNemar's test for dependent samples. The area under the curve was calculated for the thresholds using the trapezoidal rule. Because age is a strong determinant of risk score, we stratified the analysis by age greater than 50 to evaluate whether the discrimination metrics differed by age category.

Statistical significance was defined as a p-value <0.05. All analyses used Stata 13.1 (StataCorp, College Station, TX).

## Results

### Demographic and clinical characteristics

Table 1 shows the distribution of relevant demographic and clinical characteristics by HIV serostatus. The HIV-infected men (n= 599, 61% of sample) were younger and more likely to report being Hispanic/Other or African-American race. The HIV-infected men had higher fasting glucose and were more likely to have diabetes, lower total, HDL- and LDL-cholesterol, higher triglycerides, and lower body mass index (BMI). The HIV-infected men were more likely to be current smokers and to have hepatitis C virus (HCV) co-infection.

Most HIV-infected men (89%) were receiving highly active antiretroviral therapy (HAART), median duration of therapy was 9.4 years, and most participants (82%) had undetectable HIV RNA levels. Few were currently taking a regimen that included indinavir, lopinavir, or abacavir (1.0%, 8.3% and 4.3%, respectively), antiretroviral drugs in the D:A:D risk score.

Of the 975 participants included in our study sample, 975 underwent a non-contrast CT (974 non-contrast CT results available; 1 scan was technically limited) for CAC score. Coronary CT angiography was performed in 749 out of 975 (77% of the total).

The distribution of the risk categories for study participants by HIV serostatus is shown in Figure 1 for each CVD risk score algorithm, stratified by age. As expected, men older than 50 years were more likely to be classified as high risk. More HIV-infected compared to uninfected men were classified as high risk in both age groups and across risk algorithms, except for the PCE among men older than 50 years, which categorized two-thirds of evaluated men as high risk, regardless of HIV serostatus. Among younger men, the D:A:D risk score classified fewer HIV-infected men as low risk and more as moderate risk compared to the two general population risk categories; it classified fewer as high risk compared to the PCE but more than the FRS for men older than 50 years. Regardless of HIV serostatus, more men were classified as high risk by the PCE.

### Association of PCE Category with Coronary Plaque by HIV Serostatus

We expected that plaque presence would be higher in moderate/high risk men compared to the low risk men, which was generally true (Table 2). For example, odds of CAC>0 among high-risk HIV-infected men was three times higher than low-risk HIV-infected men (OR 3.13, p<0.001). Odds of CAC>0 was even higher among high risk HIV-uninfected men

compared with low risk HIV-uninfected men (OR of 7.03 (p<0.001)). The risk group-HIV interaction was statistically significant (p value =0.01).

Similarly, for the presence of any plaque on coronary CT angiography, mixed plaque, and coronary stenosis    50%, we observed higher odds of these outcomes in moderate risk men compared to low risk men and in high risk men compared to low risk men. Among those outcomes, the high risk category was more strongly associated with plaque presence among HIV-uninfected compared to HIV-infected men (only statistically significant for mixed plaque (p=0.04)).

In contrast to other plaque outcomes, the high risk category was more strongly associated with non-calcified plaque in HIV-infected men compared to uninfected men (OR 3.26, 95% CI 2.08, 5.12, v. 2.09, 95% CI 1.24, 3.52; interaction not significant).

For each plaque outcome, plaque prevalence in the low risk group was higher among HIV-infected than HIV-uninfected men, though the differences were not statistically significant. For example, 36.0% of low risk HIV-infected participants had CAC>0 compared to 26.5% of low risk HIV-uninfected men (p-value = 0.09) (see Table, Supplemental Digital Content 3, comparing odds of plaque by HIV serostatus among men categorized as low risk).

### Association of Framingham Risk Score with plaque by HIV status

The corollary results using the FRS categories are shown (see Table, Supplemental Digital Content 4, showing the FRS category—coronary plaque by HIV serostatus). Again, for each plaque outcome, the plaque prevalence in the low risk group was higher in the HIV-infected compared to the HIV-uninfected group. For example, 41.6% of low risk HIV-infected men had CAC>0 compared to 36.0% of low risk HIV-uninfected men. More participants characterized as low risk with the FRS had plaque, compared with men characterized as low risk with the PCE, the result of more men being categorized as low risk with the FRS compared with the pooled cohort.

As described in the prior section, the odds of plaque generally increased with increasing PCE risk category, with the odds ratio for the men in the high risk category greater than the odds ratio for the men in the moderate risk category. However, the increase in odds with increasing FRS risk category was not as consistent. This is the result of few men being categorized as high risk with the FRS. When moderate/high risk category men are considered in a combined fashion for PCE and FRS, odds of plaque are consistently higher compared with low risk category men.

Again, the associations with non-calcified plaque did not follow the pattern observed with other outcomes. The odds of non-calcified plaque among high-risk HIV-infected men was over three times higher than low-risk HIV-infected men (OR 3.19, p<0.001). However, the odds of non-calcified plaque among HIV-uninfected men in the high risk category compared to the low risk category was 1.39 (p=0.08) (risk score-HIV interaction not significant).

We also evaluated the discrimination of the continuous risk scores for the presence of coronary plaque. The ROC curves plot the ability of the scores to separate those with and without coronary plaque (CAC>0 and stenosis>=50%) using each observed PCE risk score

value as a threshold associated with a sensitivity (y-axis) and 1-specificity (x-axis for CAC>0) (Figure 2). The area under the ROC curve is significantly higher for the HIV-uninfected compared to HIV-infected men for CAC>0 (0.75 vs 0.65, p<0.01) and marginally higher for coronary stenosis (0.69 vs 0.59, p=0.06). Across the range of PCE risk scores for HIV-infected men, a cutpoint with a given level of sensitivity will have worse specificity in the HIV-infected compared to HIV-uninfected men. The ROC curves are similar for the FRS (data not shown). Despite the relative higher performance of the scores among the HIV-uninfected men, the areas under the ROC curve are less than 0.8, a commonly cited threshold for sufficient discrimination, regardless of serostatus.

### D:A:D compared to general population CVD risk score categories

Our secondary objective was to evaluate whether the D:A:D score better classified plaque presence than the general population score categories in the HIV-infected men. Table 3 shows that the high risk category by PCE identified the most men with plaque and stenosis 50%, though its specificity was lower than the D:A:D and Framingham. For example, among men > 50 years, the high risk category included 71.4% of men with CAC>0 using the PCE, compared to 40.5% with CAC>0 using the D:A:D and just 24.7% with CAC>0 using the FRS (p<0.001 comparing each to pooled cohort). For men    50 years, the high risk category captured fewer of those with atherosclerosis for each respective risk equation (e.g., for CAC>0, sensitivity was 31.8% with the PCE, 17% with FRS, and 15.9% with D:A:D). Conversely, the specificity of the PCE high risk category was lower compared with D:A:D and FRS (e.g., among men > 50 years old for CAC>0, 41.1% for pooled cohort, 69.4% for D:A:D, and 74.2% for FRS). The gains in sensitivity when combining the moderate/high risk categories are sizeable, particularly for the D:A:D, which classifies the largest proportion of men with plaque as moderate risk, as shown in Figure 1. When considering moderate/high as a combined group, the D:A:D has significantly greater sensitivity than the PCE and FRS. None of the risk score categories had both high sensitivity and specificity, and the area under the curves indicated inadequate discrimination (<70%) of all three scores among HIV-infected men.

The prevalence of any plaque was high among the older HIV-infected men classified as low risk using each of the three scores: 86% (81/94) by FRS, 82% (27/33) by pooled cohort, and 91% (10/11) by D:A:D (see Figure, Supplemental Digital Content 5). Despite the similar prevalence across algorithms, the absolute number of men with plaque who are classified as having low risk of cardiovascular outcomes (false negatives), was minimized with the D:A:D, which classifies fewer HIV-infected men as low risk. Among the men aged 50 and younger, the prevalence of any plaque among the men in the low risk category was significantly lower in the D:A:D (41%, 19/46) versus the FRS (60%, 86/143) and marginally lower versus the pooled cohort algorithm (58%, 65/113).

## Discussion

In this large, well-characterized group of HIV-infected and uninfected men, moderate and high risk general population score categories (FRS and PCE) were more strongly associated with plaque presence among HIV-uninfected men than among HIV-infected men. Among

HIV-infected men, the PCE high risk category was more sensitive for plaque presence than both the D:A:D and the FRS, however, the specificity was lower. Current ACC/AHA CVD risk reduction guidelines recommend statin therapy for patients in the PCE high risk category, and our results show that for HIV-infected men aged 50 and younger, this will miss most men with plaque and most men with stenosis 50%. In both age groups, stenosis 50% represents a potentially high risk lesion that could lead to ischemia. CAC>0 is predictive of CVD events compared to CAC=0 [19], with the significance of a particular lesion depending on both the degree of CAC and patient's age.

In previous work, FRS and PCE have both been shown to underestimate risk for cardiac events [9, 20, 21] and subclinical atherosclerosis assessed by carotid IMT [10, 13] in HIV-infected persons. The D:A:D score has performed better than general population scores in some studies in predicting myocardial infarction [9] and carotid IMT [13] among HIV-infected people. However, an analysis of HIV Outpatient Study (HOPS) data revealed more observed CVD events than expected by the D:A:D score, with a ratio of expected events to observed events of 0.75. The ratio of expected events to observed events was higher using the FRS (0.85) and the PCE (0.83) [21]. Our study did not show any advantage of the D:A:D score over the general population risk scores for the intermediate outcome of coronary plaque. D:A:D high risk category was not very sensitive for plaque in either age group examined, and when the moderate/high risk groups were combined (versus the low risk group), although the sensitivity increased to include almost all of the men with plaque, specificity dropped sharply.

Chronic effects of HIV infection itself (inflammation, hypercoagulability, endothelial dysfunction), effects of certain ART drugs (hyperlipidemia, insulin resistance), lifestyle risk factors, particularly smoking, and other chronic medical comorbidities (hypertension, diabetes, and hyperlipidemia) [22–25] all contribute to CVD risk among HIV-infected persons. Some factors that contribute to increased risk of CVD among HIV-infected patients (e.g. chronic inflammation) are not incorporated into risk prediction scores [11, 26]. The D:A:D score accounts for certain ART agents (abacavir, indinavir, and lopinavir) that contribute to cardiovascular risk independent of the metabolic derangement expected with any ART [27–30]. However, this adjustment was of limited importance in our study population with low levels of use of these ART agents. The D:A:D uses an algorithm that weights the effects of traditional risk factors such as age and hypertension based on their associations with cardiovascular outcomes in an HIV-infected rather than the general population. Even so, we did not see an enhanced performance of the D:A:D compared to the general population risk scores in our analysis. Because the upper threshold for the low risk category (<1% 5-year risk) is so low, few people are classified in the low risk group, contributing to the score's low specificity.

The strengths of our study include a large sample size with standardized collection of CV risk factors from which to calculate risk scores and the presence of an HIV-uninfected comparison group. We classified subclinical coronary atherosclerosis using coronary CT angiography, which is a very specific and sensitive measure. Limitations of our study include the cross sectional analysis and the limited number of hard coronary outcomes, preventing us from looking at associations between risk scores and hard coronary endpoints

over time. CVD risk scores were developed to predict hard coronary outcomes, not subclinical CVD, and therefore we might not expect very high discrimination metrics for our intermediate outcomes. However, both CAC and plaque have been associated with subsequent coronary events [19, 31–33]. In a large study of outpatients undergoing coronary CTA, cumulative probability of a major coronary endpoint increased with the degree of CAC from 2.1% among individuals with a CAC of 0 to 16.3% among individuals with a CAC > 400. No plaque was associated with cumulative probability of major adverse cardiac events of 0.8% and cumulative probability of event increased as the number of involved vessels increased. Calcified plaque had the lowest risk of subsequent event (5.5%), while noncalcified and mixed plaque had the highest (22.7% and 37.7%, respectively) [19]. In another study examining plaque characteristics among individuals with acute coronary syndrome, noncalcified plaque presence was two-fold higher comparing ACS with non-ACS group members (43% vs. 22%, p < 0.01) [33]. There was variation in the prevalence of our plaque outcomes, with mixed plaque and coronary stenosis >50% being the least prevalent. Even with the lower prevalence, we observed a stronger risk score-plaque association for these outcomes among HIV-uninfected men when general population risk scores were used.

In summary, risk score-plaque associations for the general population risk scores were weaker among HIV-infected men compared with HIV-uninfected men, except for non-calcified plaque. The high risk category by PCE identified the greatest percent of men with plaque, regardless of serostatus, however, with very low specificity. No risk score delivered both high sensitivity and specificity among HIV-infected men. Clinicians must balance the limitations of each of the scores, and the risk of side effects with statin therapy, when making individual treatment decisions for their patients.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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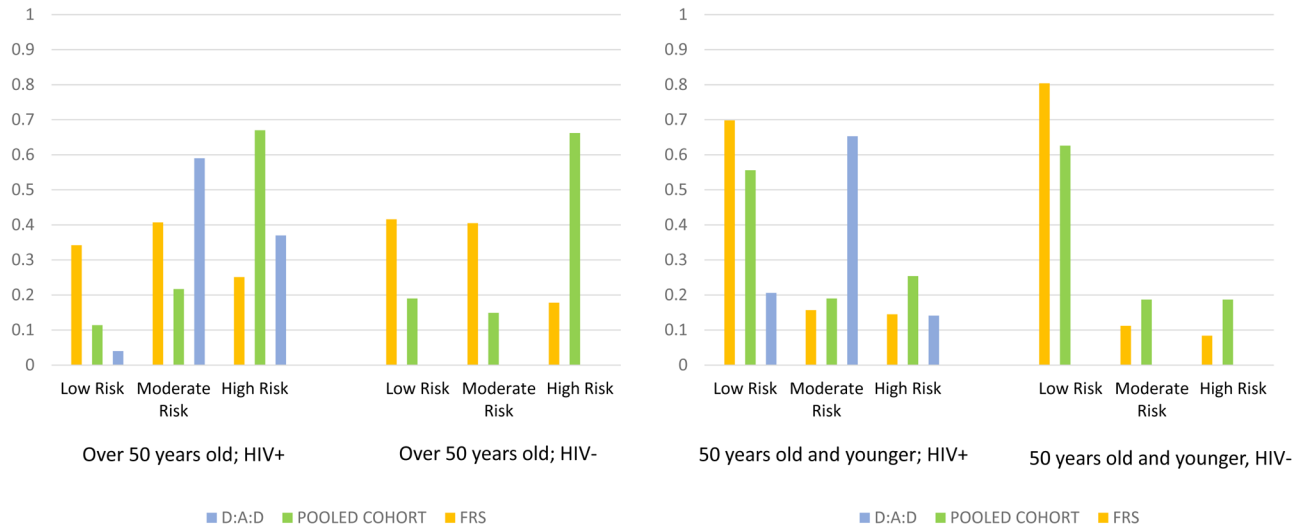
**Figure 1.**
Distribution of the Categories of 10 Year CVD Risk* by HIV Status for the three Risk
Scores among MACS Participants, 2010–2013, stratified by age

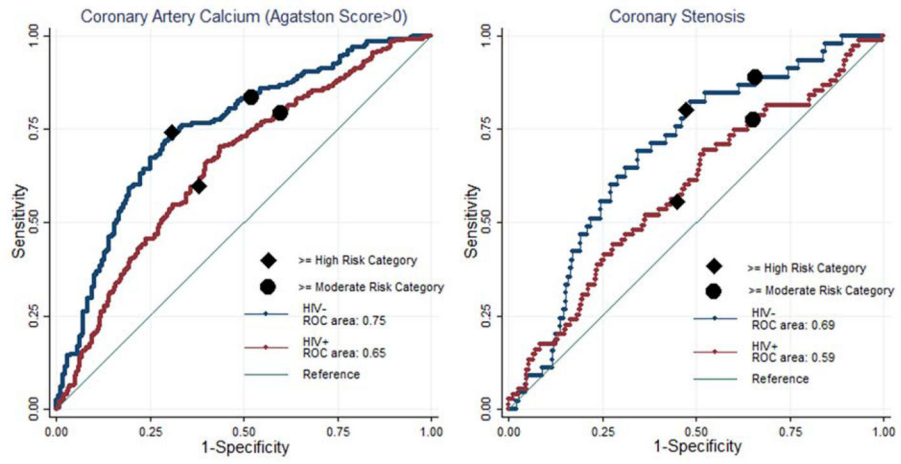**Figure 2.**

**Table 1**

Descriptive Characteristics of the MACS Participants, by HIV Status, 2010–2013

| | HIV+ n=599 | HIV– n=376 | P-value |
|---|---|---|---|
| Age (years) | 52 (47, 58) | 54 (50, 61) | **<0.001** |
| Race | | | **<0.001** |
|    Caucasian | 315 (52.6%) | 253 (67.3%) | |
|    Hispanic/Other | 80 (13.4%) | 32 (8.5%) | |
|    African-American | 204 (34.1%) | 91 (24.2%) | |
| Systolic Blood Pressure (mmHg) | 126 (115, 137) | 128 (118, 137) | 0.24 |
| On Hypertensive Medications | 212 (35.4%) | 116 (30.9%) | 0.14 |
| Fasting Glucose (mg/dL) | 98 (90, 108) | 96 (89, 105) | **0.02** |
| Diabetes (1) | 109 (18.2%) | 49 (13.0%) | **0.03** |
| Total Cholesterol (mg/dL) | 185 (157, 212) | 190 (167, 216) | **0.03** |
| HDL-Cholesterol (mg/dL) | 46 (38, 55) | 52 (42, 60) | **<0.001** |
| LDL-Cholesterol (mg/dL) | 104 (82, 129) | 112 (91, 137) | **<0.001** |
| Triglycerides (mg/dL) | 132 (95, 201) | 104 (74, 147) | **<0.001** |
| On Lipid Lowering Medications | 202 (34.6%) | 111 (30.0%) | 0.14 |
| Body Mass Index (kg/m$^2$) | 26 (23, 28) | 27 (24, 30) | **<0.001** |
| Smoking Status | | | **<0.01** |
|    Current | 183 (30.6%) | 82 (21.8%) | |
|    Former | 265 (44.2%) | 201 (53.5%) | |
|    Never | 151 (25.2%) | 93 (24.7%) | |
| Hepatitis C Infection | 66 (11.0%) | 17 (4.5%) | **<0.001** |
| **HIV-specific factors** | | | |
| Undetectable Viral Load (< 50 copies) | 491 (82.0%) | | |
| HIV RNA (copies/mL)(2) | 661 (139, 19500) | | |
| On HAART | 530 (88.5%) | | |
| Time on HAART (years) | 9.4 (6.3, 12.4) | | |
| Current Indinavir use | 6 (1.0%) | | |
| Indinavir exposure (years) | 0.0 (0.0, 0.8) | | |
| Current Lopinavir use | 50 (8.3%) | | |
| Lopinavir exposure (years) | 0.0 (0.0, 0.8) | | |
| Current Abacavir | 26 (4.3%) | | |
| CD4+ T-cell count (cells/mm$^3$) | 594 (419, 765) | | |
| CD4+ T-cell nadir (cells/mm$^3$) | 284 (172, 399) | | |
| History of AIDS | 89 (14.9%) | | |

HDL= high-density lipoprotein, LDL = low-density lipoprotein, HAART = highly active antiretroviral therapy. Prevalence (%) or median and interquartile range. P-values determined using the Wilcoxon rank sum or chi-square test as appropriate. (1) Diabetes was defined as having a fasting glucose >=126 or being on diabetes medication, either at the current visit, or at two or more previous visits (2) HIV viral load among the 109 HIV+ men with detectable current HIV RNA (>50 copies/mL) levels.

**Table 2**

Association between ACC/AHA Pooled Cohort Equation Risk Categories and Coronary Plaque by HIV serostatus, among men in the MACS, 2010–2013

| | HIV-infected (n=445 CTA/n=599 CT) | | | HIV-uninfected (n=304 CTA/n=375 CT) | | | Interaction p-value |
|---|---|---|---|---|---|---|---|
| | N | % | OR and 95% CI | N | % | OR and 95% CI | |
| **CAC>0** | | | | | | | |
| Low Risk | 178 | 36.0% | 1 (ref) | 117 | 26.5% | 1 (ref) | |
| Moderate Risk | 123 | 49.6% | 1.75 * [1.10,2.80] | 60 | 36.7% | 1.61 [0.82,3.13] | 0.83 |
| High Risk | 298 | 63.8% | 3.13 *** [2.13,4.61] | 198 | 71.7% | 7.03 *** [4.21,11.76] | 0.01 |
| **Any Plaque on CCTA** | | | | | | | |
| Low Risk | 146 | 63.0% | 1 (ref) | 93 | 52.7% | 1 (ref) | |
| Moderate Risk | 91 | 76.9% | 1.96 * [1.08,3.54] | 52 | 69.2% | 2.02 [0.99,4.13] | 0.95 |
| High Risk | 208 | 88.0% | 4.30 *** [2.51,7.35] | 159 | 89.3% | 7.50 *** [3.93,14.33] | 0.19 |
| **Non Calcified Plaque Presence** | | | | | | | |
| Low Risk | 146 | 47.3% | 1 (ref) | 93 | 40.9% | 1 (ref) | |
| Moderate Risk | 91 | 61.5% | 1.79 * [1.05,3.04] | 52 | 55.8% | 1.82 [0.92,3.62] | 0.96 |
| High Risk | 208 | 74.5% | 3.26 *** [2.08,5.12] | 159 | 59.1% | 2.09 ** [1.24,3.52] | 0.21 |
| **Mixed Plaque Presence** | | | | | | | |
| Low Risk | 146 | 24.7% | 1 (ref) | 93 | 15.1% | 1 (ref) | |
| Moderate Risk | 91 | 36.3% | 1.74 [0.98,3.07] | 52 | 21.2% | 1.51 [0.63,3.63] | 0.80 |
| High Risk | 208 | 39.4% | 1.99 ** [1.25,3.18] | 159 | 45.3% | 4.67 *** [2.44,8.93] | 0.04 |
| **Coronary Stenosis >=50%** | | | | | | | |
| Low Risk | 146 | 11.6% | 1 (ref) | 93 | 5.4% | 1 (ref) | |
| Moderate Risk | 91 | 17.6% | 1.62 [0.77,3.39] | 52 | 7.7% | 1.47 [0.38,5.72] | 0.90 |
| High Risk | 208 | 20.2% | 1.92 * [1.04,3.53] | 159 | 22.6% | 5.15 *** [1.94,13.65] | 0.09 |

Exponentiated coefficients; 95% confidence intervals in brackets

*
$p < 0.05$,

**
$p < 0.01$,

***
$p < 0.001$

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**Table 3**

Discrimination metrics of the D:A:D, Framingham Hard CVD Risk Categories, and pooled cohort equation for coronary plaque by age strata, among HIV-infected men in the MACS, 2010–2013

| | | N with plaque | Sensitivity 95% CI | | | N without plaque | Specificity 95% CI | | | Area under the ROC curve | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | D:A:D | FRS | PCE | | D:A:D | FRS | PCE | D:A:D | FRS | PCE |
| **≤50 years of age (n=201 CTA/n=248 CT)** | | | | | | | | | | | | |
| CAC>0 | Moderate Risk Category | 88 | 87.5% (78.7,93.6) | 34.1% (24.3,45.0) *** | 48.9% (38.1,59.8) *** | 160 | 25.0% (18.5,32.4) | 71.9% (64.2,78.7) *** | 58.1% (50.1,65.9) *** | 0.56 | 0.53 | 0.55 |
| | High Risk Category | | 15.9% (9.0,25.2) | 17.0% (9.9,26.6) | 31.8% (22.3,42.6) *** | | 86.9% (80.6,91.7) | 86.9% (80.6,91.7) | 78.1% (70.9,84.3) * | | | |
| Any plaque on CTA | Moderate Risk Category | 129 | 85.3% (78.0,90.9) | 33.3% (25.3,42.2) *** | 49.6% (40.7,58.5) *** | 72 | 37.5% (26.4,49.7) | 79.2% (68.0,87.8) *** | 66.7% (54.6,77.3) *** | 0.64 | 0.57 | 0.59 |
| | High Risk Category | | 17.1% (11.0,24.7) | 16.3% (10.4,23.8) | 30.2% (22.5,38.9) *** | | 94.4% (86.4, 98.5) | 94.4% (86.4, 98.5) | 84.7% (74.3,92.1) * | | | |
| Non-calcified plaque | Moderate Risk Category | 97 | 84.5% (75.8,91.1) | 38.1% (28.5,48.6) *** | 53.6% (43.2,63.8) *** | 104 | 29.8% (21.2,39.6) | 79.8% (70.8,87.0) *** | 65.4% (55.4,74.4) *** | 0.60 | 0.60 | 0.61 |
| | High Risk Category | | 18.6% (11.4,27.7) | 20.6% (13.1,30.0) | 33.0% (23.8,43.3) | | 92.3% (85.4,96.6) | 95.2% (89.1, 98.4) | 82.7% (74.0,89.4) ** | | | |
| Stenosis > 50% | Moderate Risk Category | 18 | 77.8% (52.4,93.6) | 44.4% (21.5,69.2) * | 44.4% (21.5,69.2) * | 183 | 23.0% (17.1,29.7) | 72.7% (65.6, 79.0) *** | 56.3% (48.8,63.6) *** | 0.54 | 0.61 | 0.52 |
| | High Risk Category | | 22.2% (6.4,47.6) | 33.3% (13.3,59.0) | 33.3% (13.3,59.0) | | 88.0% (82.4,92.3) | 89.6% (84.3,93.6) *** | 76.0% 69.1,82.0) *** | | | |
| **>50 years of age (n=244 CTA/n=351 CT)** | | | | | | | | | | | | |
| CAC>0 | Moderate Risk Category | 227 | 96.9% (93.7,98.8) | 71.8% (65.5, 77.6) *** | 91.6% (87.2,94.9) ** | 124 | 5.6% (2.3,11.3) | 45.2% (36.2,54.3) *** | 16.9% (10.8,24.7) ** | 0.56 | 0.56 | 0.57 |
| | High Risk Category | | 40.5% (34.1,47.2) | 24.7% (19.2,30.8) *** | 71.4% (65.0,77.2) *** | | 69.4% (60.4,77.3) | 74.2% (65.6,81.6) | 41.1% (32.4,50.3) *** | | | |
| Any plaque on CTA | Moderate Risk Category | 216 | 95.4% (91.7,97.8) | 62.5% (55.7,69.0) *** | 87.5% (82.3,91.6) *** | 28 | 3.6% (0.1,18.3) | 46.4% (27.5,66.1) *** | 21.4% (8.3,41.0) | 0.56 | 0.50 | 0.59 |
| | High Risk Category | | 33.8% (27.5,40.5) | 19.9% (14.8,25.9) *** | 66.7% (60.0,72.9) *** | | 78.6% (59.0,91.7) | 67.9% (47.6,84.1) | 50.0% (30.6,69.4) * | | | |
| Non-calcified plaque | Moderate Risk Category | 183 | 95.6% (91.6,98.1) | 62.3% (54.8,69.3) *** | 86.9% (81.1,91.4) *** | 61 | 4.9% (1.0,13.7) | 41.0% (28.6,54.3) *** | 14.8% (7.0,26.2) * | 0.52 | 0.53 | 0.55 |
| | High Risk Category | | 33.3% (26.6,40.7) | 22.4% (16.6,29.1) ** | 67.2% (59.9,74.0) *** | | 70.5% (57.4,81.5) | 82.0% (70.0,90.6) | 42.6% (30.0,55.9) ** | | | |
| Stenosis > 50% | Moderate Risk Category | 57 | 96.2% (90.6,99.0) | 64.9% (51.1,77.1) *** | 87.7% (76.3,94.9) * | 187 | 5.1% (2.1,10.2) | 39.6% (32.5,47.0) *** | 13.9% (9.3,19.7) *** | 0.56 | 0.52 | 0.49 |
| | High Risk Category | | 40.4% (27.6,54.2) | 22.8% (12.7, 35.8) ** | 63.2% (49.3,75.6) ** | | 70.1% (62.9, 76.5) | 79.1% (72.6,84.7) * | 34.8% (28.0,42.1) *** | | | |

Difference in the sensitivity and specificity of the FRS and pooled cohort equation, each compared to the D:A:D was assessed using McNemar's test;

*
p < 0.05,

**
p < 0.01,

***
$p < 0.001$