**APPENDIX**

**Additional details on study setting**

The Women's Interagency HIV Study (WIHS) was initiated in 1994 and has enrolled over 4,000 women at six U.S. sites: Bronx, New York; Brooklyn, New York; Chicago, Illinois; Los Angeles, California; San Francisco, California; and Washington, D.C.  Recruitment in the WIHS occurred in three waves (1994-1995, 2001-2002, and 2010-2012) from HIV primary care clinics, hospital-based programs, community outreach, support groups, and other locations.

The Multicenter AIDS Cohort Study (MACS) was initiated in 1984, and has enrolled approximately 7,000 gay or bisexual men from four U.S. sites: Baltimore, Maryland; Chicago, Illinois; Los Angeles, California; and Pittsburgh, Pennsylvania.  MACS recruitment also occurred in three waves (1984-1985, 1987, and 2001-2003).

Additional details on study design are published.(1-4)  Briefly, each study has semi-annual follow-up visits, during which participants undergo similar detailed examinations, specimen collection, and structured interviews assessing health behaviors, medical history, and medication use.

**Additional details on inclusion and exclusion criteria**

All WIHS participants were eligible for participation in the vascular substudy at the time of recruitment; MACS participation was restricted to men reporting no history of coronary heart disease (CHD).  Additional exclusion criteria for MACS participants were age <40 years and weight >300 pounds, because the MACS vascular substudy also included coronary artery

calcium measurements,(5, 6) which provide little information among younger individuals and, for technical reasons, are difficult to perform in the morbidly obese.
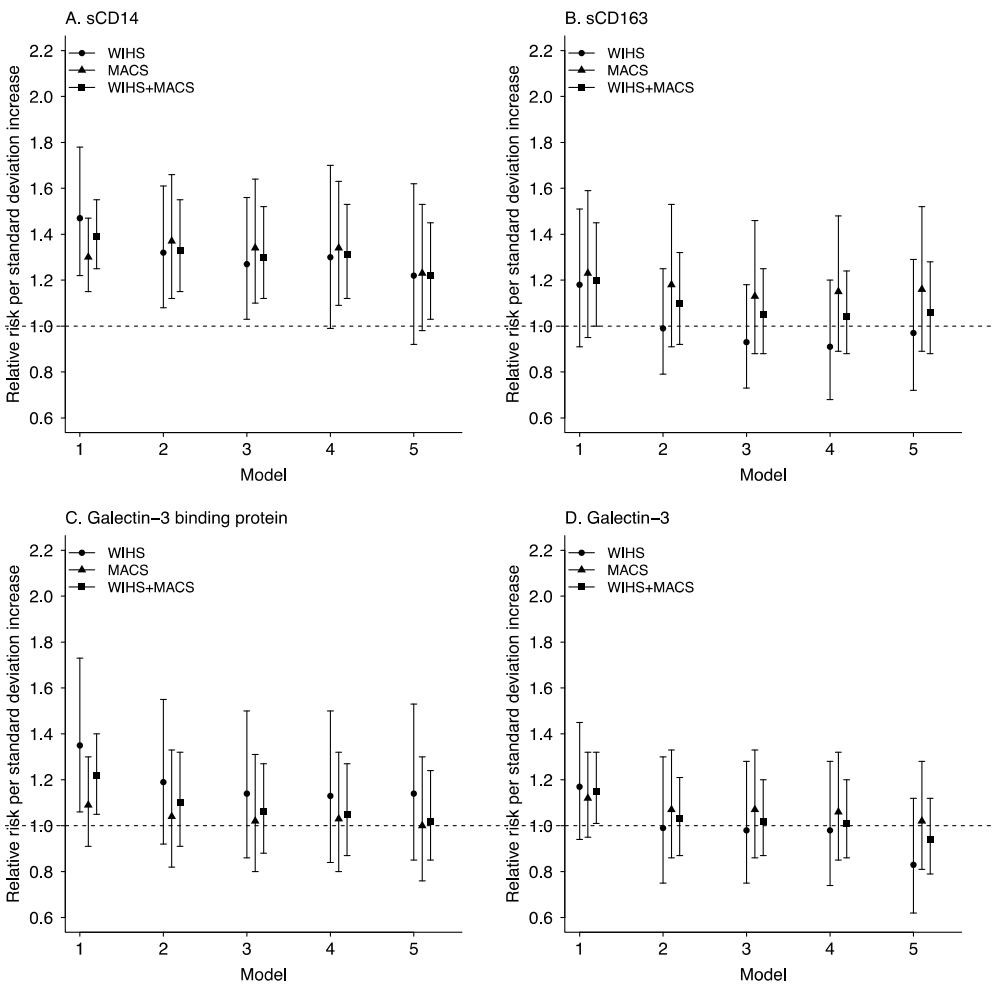
For the present analyses, we excluded WIHS participants with a reported history of CHD (N=138) for consistency with the MACS.  We also excluded 10 individuals who acquired HIV during the study period, 2004-2013.

**References**

1.	Barkan SE, Melnick SL, Preston-Martin S, et al. The Women's Interagency HIV Study. Epidemiology **1998**; 9: 117-125.

2.	Bacon MC, von Wyl V, Alden C, et al. The Women's Interagency HIV Study: An observational cohort brings clinical sciences to the bench. Clin Diagn Lab Immunol **2005**; 12: 1013-1019.

3.	Kaslow RA, Ostrow DG, Detels R, Phair JP, Polk BF, Rinaldo CR, Jr. The Multicenter AIDS Cohort Study: rationale, organization, and selected characteristics of the participants. Am J Epidemiol **1987**; 126: 310-318.

4.	Silvestre AJ, Hylton JB, Johnson LM, et al. Recruiting minority men who have sex with men for HIV research: results from a 4-city campaign. Am J Public Health **2006**; 96: 1020-1027.

5.	Kingsley LA, Cuervo-Rojas J, Munoz A, et al. Subclinical coronary atherosclerosis, HIV infection and antiretroviral therapy: Multicenter AIDS Cohort Study. AIDS **2008**; 22: 1589-1599.

6.	Post WS, Budoff M, Kingsley L, et al. Associations between HIV infection and subclinical coronary atherosclerosis. Ann Intern Med **2014**; 160: 458-467.

**Supplemental Figure 1. Association between monocyte/macrophage markers and formation of new focal carotid artery plaque among HIV-infected participants, overall and by cohort, for (A) sCD14, (B) sCD163, (C) galectin-3 binding protein, and (d) galectin-3.**
Symbols represent relative risk and error bars represent 95% confidence intervals. Model 1 unadjusted; Model 2 additionally adjusted for age, race/ethnicity, income, education, study site, current smoking, current crack/cocaine use, current alcohol use, history of injection drug use, and history of hepatitis C virus infection; Model 3 additionally adjusted for baseline CD4+ T-cell count and ART use; Model 4 additionally adjusted for hsCRP and IL-6; Model 5 additionally adjusted for body mass index, systolic blood pressure, total and HDL cholesterol, use of anti-hypertension or anti-cholesterol medications, history of diabetes, eGFR.

**Supplemental Table 1.  Levels of monocyte and macrophage markers, by cohort and new focal plaque formation.**

| | Women's Interagency HIV Study (WIHS) | | | Multicenter AIDS Cohort Study (MACS) | | | WIHS and MACS combined | | |
|---|---|---|---|---|---|---|---|---|---|
| | New plaque formation (N=86) Median (IQR) | No new plaque (N=692) Median (IQR) | P-value | New plaque formation (N=112) Median (IQR) | No new plaque (N=391) Median (IQR) | P-value | New plaque formation (N=198) Median (IQR) | No new plaque (N=1,083) Median (IQR) | P-value |
| Soluble CD14 (ng/mL) | 2,146 (1,883-2,582) | 1,895 (1,569-2,295) | <0.001 | 2,097 (1,779-2,468) | 1,869 (1,617-2,227) | <0.001 | 2,112 (1,819-2,534) | 1,886 (1,585-2,267) | <0.001 |
| Soluble CD163 (ng/mL) | 865 (650-1,239) | 826 (582-1,115) | 0.16 | 783 (598-995) | 629 (487-867) | <0.001 | 805 (601-1,092) | 741 (539-1,037) | 0.03 |
| Galectin-3 binding protein (µg/mL) | 15.2 (7.6-25.7) | 10.4 (6.5-18.0) | 0.005 | 6.1 (3.8-9.7) | 5.2 (3.4-8.6) | 0.04 | 7.9 (4.8-16.8) | 8.0 (4.7-15.0) | 0.49 |
| Galectin-3 (ng/mL) | 9.5 (7.5-12.0) | 8.9 (7.1-11.0) | 0.13 | 8.9 (7.3-10.4) | 8.2 (6.9-10.1) | 0.08 | 9.1 (7.5-11.0) | 8.6 (7.0-10.6) | 0.11 |
| High sensitivity C-reactive protein (µg/mL) | 2.6 (0.9-5.5) | 2.4 (0.9-5.7) | 0.91 | 1.4 (0.7-3.2) | 1.1 (0.5-2.5) | 0.09 | 1.7 (0.7-4.4) | 1.8 (0.7-4.8) | 0.83 |
| Interleukin-6 (pg/mL) | 1.1 (0.8-2.1) | 0.9 (0.6-1.5) | 0.02 | 0.9 (0.6-1.5) | 0.8 (0.5-1.4) | 0.14 | 1.0 (0.7-1.6) | 0.9 (0.6-1.5) | 0.03 |

**Supplemental Table 2.  Adjusted association between monocyte/macrophage markers and formation of new focal carotid artery plaque, overall and by cohort.**

| Marker | Women's Interagency HIV Study (WIHS) Risk ratio (95% confidence interval) | P-value | Multicenter AIDS Cohort Study (MACS) Risk ratio (95% confidence interval) | P-value | WIHS and MACS combined Risk ratio (95% confidence interval) | P-value |
|---|---|---|---|---|---|---|
| N events / total | 86 / 778 | | 112 / 503 | | 198 / 1,281 | |
| sCD14 | | | | | | |
| Quartile 1 | 1.00 (Ref) | - | 1.00 (Ref) | - | 1.00 (Ref) | - |
| Quartile 2 | 2.68 (1.06-6.79) | 0.04 | 1.54 (0.80-2.95) | 0.19 | 1.89 (1.13-3.17) | 0.02 |
| Quartile 3 | 3.14 (1.24-7.99) | 0.02 | 2.16 (1.13-4.12) | 0.02 | 2.35 (1.40-3.93) | 0.001 |
| Quartile 4 | 3.01 (1.17-7.76) | 0.02 | 1.70 (0.85-3.39) | 0.13 | 2.04 (1.19-3.47) | 0.01 |
| Each increase in quartile | 1.26 (1.00-1.60) | 0.05 | 1.19 (0.97-1.46) | 0.10 | 1.20 (1.03-1.40) | 0.02 |
| sCD163 | | | | | | |
| Quartile 1 | 1.00 (Ref) | - | 1.00 (Ref) | - | 1.00 (Ref) | - |
| Quartile 2 | 0.97 (0.51-1.83) | 0.92 | 1.36 (0.69-2.65) | 0.37 | 1.18 (0.75-1.85) | 0.49 |
| Quartile 3 | 0.72 (0.35-1.47) | 0.36 | 2.38 (1.30-4.36) | 0.01 | 1.49 (0.96-2.31) | 0.07 |
| Quartile 4 | 0.82 (0.41-1.66) | 0.58 | 2.02 (1.07-3.82) | 0.03 | 1.40 (0.89-2.22) | 0.15 |
| Each increase in quartile | 0.92 (0.73-1.16) | 0.48 | 1.29 (1.06-1.56) | 0.01 | 1.13 (0.98-1.30) | 0.10 |
| Galectin-3 binding protein | | | | | | |
| Quartile 1 | 1.00 (Ref) | - | 1.00 (Ref) | - | 1.00 (Ref) | - |

| | | | | | | |
|---|---|---|---|---|---|---|
| Quartile 2 | 0.70 (0.33-1.45) | 0.33 | 0.90 (0.50-1.63) | 0.72 | 0.84 (0.53-1.33) | 0.45 |
| Quartile 3 | 1.01 (0.53-1.95) | 0.97 | 1.14 (0.64-2.02) | 0.66 | 1.12 (0.73-1.71) | 0.60 |
| Quartile 4 | 1.27 (0.63-2.53) | 0.50 | 1.01 (0.53-1.90) | 0.98 | 1.10 (0.69-1.74) | 0.69 |
| Each increase in quartile | 1.11 (0.88-1.40) | 0.36 | 1.03 (0.84-1.26) | 0.77 | 1.06 (0.91-1.23) | 0.43 |
| Galectin-3 | | | | | | |
| Quartile 1 | 1.00 (Ref) | - | 1.00 (Ref) | - | 1.00 (Ref) | - |
| Quartile 2 | 0.88 (0.45-1.73) | 0.71 | 1.05 (0.58-1.90) | 0.88 | 0.96 (0.62-1.48) | 0.85 |
| Quartile 3 | 0.70 (0.35-1.42) | 0.33 | 1.22 (0.70-2.12) | 0.48 | 0.99 (0.65-1.52) | 0.97 |
| Quartile 4 | 0.68 (0.33-1.38) | 0.28 | 0.96 (0.54-1.71) | 0.88 | 0.88 (0.57-1.37) | 0.58 |
| Each increase in quartile | 0.87 (0.69-1.10) | 0.25 | 1.00 (0.84-1.20) | 0.99 | 0.97 (0.84-1.11) | 0.62 |

Model adjusted for HIV serostatus, age, race/ethnicity, education, income, study site, history of injection drug use, crack/cocaine use, current smoking, current alcohol use, history of HCV, hsCRP, IL-6, body mass index, systolic blood pressure, total and HDL cholesterol, use of anti-hypertension or anti-cholesterol medications, history of diabetes, eGFR.  P-value associated with increase in quartile represents linear trend test.

**Supplemental Table 3. Adjusted association of HIV infection, systemic inflammation markers, and other risk factors with formation of new focal carotid artery plaque, overall and by cohort.**

| Marker | Women's Interagency HIV Study (WIHS) Risk ratio per standard deviation (95% CI) | P-value | Multicenter AIDS Cohort Study (MACS) Risk ratio per standard deviation (95% CI) | P-value | WIHS and MACS combined Risk ratio per standard deviation (95% CI) | P-value |
|---|---|---|---|---|---|---|
| N events / total | 86 / 778 | | 112 / 503 | | 198 / 1,281 | |
| HIV infection | 1.25 (0.68-2.30) | 0.47 | 1.56 (0.95-2.54) | 0.08 | 1.55 (1.07-2.23) | 0.02 |
| hsCRP (per standard deviation) | 0.86 (0.67-1.09) | 0.21 | 1.08 (0.87-1.33) | 0.50 | 1.02 (0.87-1.19) | 0.83 |
| IL-6 (per standard deviation) | 1.17 (0.96-1.43) | 0.12 | 1.00 (0.80-1.23) | 0.98 | 1.07 (0.93-1.24) | 0.33 |
| Age (per year) | 1.04 (1.01-1.07) | 0.01 | 1.01 (0.97-1.05) | 0.57 | 1.03 (1.01-1.06) | 0.003 |
| Race/ethnicity (ref: white or other) | | | | | | |
| Black | 1.03 (0.47-2.28) | 0.94 | 1.04 (0.59-1.82) | 0.90 | 0.96 (0.62-1.49) | 0.87 |
| Hispanic | 0.78 (0.33-1.84) | 0.57 | 0.57 (0.22-1.45) | 0.23 | 0.69 (0.40-1.19) | 0.18 |
| Income (ref: income <$30,000/year) | | | | | | |
| $30,000/year or more | 0.91 (0.43-1.93) | 0.80 | 0.75 (0.47-1.19) | 0.22 | 0.79 (0.53-1.16) | 0.23 |
| Education (ref: did not complete high school) | | | | | | |
| Completed high school | 0.68 (0.39-1.20) | 0.18 | 1.34 (0.49-3.61) | 0.57 | 0.84 (0.53-1.33) | 0.45 |
| At least some college | 0.81 (0.47-1.41) | 0.46 | 1.15 (0.45-2.94) | 0.78 | 0.89 (0.57-1.39) | 0.61 |
| History of injection drug use | 0.72 (0.35-1.48) | 0.37 | 1.39 (0.65-2.95) | 0.39 | 0.89 (0.54-1.46) | 0.64 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Current crack/cocaine use | 1.05 (0.47-2.32) | 0.91 | 0.84 (0.45-1.58) | 0.60 | 1.02 (0.63-1.64) | 0.94 |
| Current alcohol use (ref. = abstainer) | | | | | | |
|   Light (<3 drinks/week, WIHS; 1-3, MACS) | 1.09 (0.81-1.46) | 0.56 | 1.32 (1.01-1.73) | 0.04 | 1.16 (0.95-1.40) | 0.14 |
|   Moderate (3-13, WIHS; 4-13 MACS) | | | | | | |
|   Heavier (14+ drinks/week) | | | | | | |
| Current smoker at baseline | 1.58 (0.96-2.60) | 0.07 | 0.98 (0.61-1.58) | 0.93 | 1.34 (0.96-1.87) | 0.08 |
| Body mass index (per kg/m$^2$) | 0.97 (0.93-1.00) | 0.06 | 0.97 (0.93-1.02) | 0.28 | 0.97 (0.94-0.99) | 0.02 |
| Systolic blood pressure (per 10 mm Hg) | 1.01 (0.89-1.16) | 0.84 | 1.09 (0.93-1.27) | 0.31 | 1.04 (0.95-1.15) | 0.41 |
| Use of anti-hypertensive medications | 1.50 (0.85-2.67) | 0.16 | 1.39 (0.88-2.22) | 0.16 | 1.41 (0.99-2.00) | 0.06 |
| Total cholesterol (per 10 mg/dL) | 1.06 (1.00-1.12) | 0.06 | 1.03 (1.00-1.07) | 0.048 | 1.04 (1.01-1.07) | 0.004 |
| HDL-cholesterol (per 10 mg/dL) | 0.95 (0.82-1.10) | 0.47 | 0.92 (0.79-1.06) | 0.25 | 0.94 (0.85-1.04) | 0.22 |
| Use of anti-cholesterol medications | 1.58 (0.74-3.38) | 0.24 | 1.23 (0.77-1.97) | 0.38 | 1.29 (0.87-1.91) | 0.21 |
| History of diabetes | 1.77 (1.06-2.94) | 0.03 | 1.25 (0.67-2.31) | 0.48 | 1.43 (0.99-2.08) | 0.06 |
| eGFR | 1.14 (0.92-1.41) | 0.22 | 1.32 (0.49-3.52) | 0.58 | 1.13 (0.94-1.36) | 0.19 |

Models adjusted for all factors listed above and study site.