HIV-infection and ART, but not high sensitivity CRP, are associated with markers of vascular function: Results from the Western Cape cohort of the EndoAfrica study.
CD4 T-helper cells are the primary cellular targets of HIV

CD4: “Cluster of differentiation 4”: Membrane-bound glycoprotein found in T-helper cells, macrophages, monocytes

Reverse transcriptase

Up to 50-billion mature HIV-1 virions replicate in CD4 cells every day during the asymptomatic phase of HIV-infection

Smith RL et al., Front. Gen.; 2013
CD4 T-helper cells: The master regulators of the adaptive immune response, are **ACTIVATED** and **DEPLETED** in HIV

- Activates Humoral Immunity
- Activates CD8 Cytotoxic T cells
- Activates Innate Immunity and Inflammatory Response
Adaptive and innate immune system activation in HIV

**ADAPTIVE**
- CD8 cells
- CD4 cells

- **Biological Action**
  - Cell Death
  - Inflammation
  - Cytokines
    - IFN-γ, TNF
    - IL-4

- **Effect on Lesions**

**INNATE**
- Monocytes / tissue Macrophages

- **Biological Action**
  - Ly6C/GR-1 High
  - TLRs
  - Proteases
  - Reactive O₂ Species
  - Nitric Oxide
  - TNF
  - IL-1
  - Other Cytokines

- **Effect on Lesions**

*Libby P et al., JACC 2009*
HIV-infection + ART

↓ HIV/AIDS-related mortality and morbidity

BUT:

↑ Risk for non-infectious and non-AIDS complications

Ageing  Residual Chronic Immune Activation  ↑Modifiable Traditional Risk factors (smoking, alcohol)  ART drugs metabolic side-effects

↑ CARDIOVASCULAR RISK

Sereti I & Altfeld M., Curr Opin HIV AIDS 2016
Time-line of HIV + ART and CVD

Pre-HAART
- Myocarditis
- Dilated cardiomyopathy
- Left ventricular dysfunction
- Pericardial effusion
- Pulmonary hypertension

Post-HAART
- Coronary artery disease
- Myocardial infarction
- Early atherosclerosis

1995: Highly Active Antiretroviral Therapy (HAART)
Pathophysiologic mechanisms of HIV underlying CVD

- HIV infection
  - HIV replication
  - Immune activation
    - CD4 and CD8
    - Inflammation
      - Endothelial function
        - Smoking hypertension
      - Inflammation
        - Macrophage recruitment
          - Insulin resistance
            - Altered lipid effects
              - HIV infection

- Atherosclerosis
  - Diabetes
  - Genetics

- Reverse cholesterol transport (foam cell development)
- Impaired HDL metabolism

Currier JS, Top HIV Med. 2009; 17(3): 98-103
Pathophysiological mechanisms of HIV underlying CVD

- HIV infection
  - HIV replication
    - Immune activation
      - Inflammation
        - Endothelial function
          - Smoking
            - Hypertension
      - Macrophage recruitment
    - Insulin resistance
  - Antiretroviral therapy effects
  - Altered lipid effects
  - HIV infection

Atherosclerosis

Currier JS, Top HIV Med. 2009; 17(3): 98-103
Pathophysiological mechanisms of HIV underlying vascular disease

**HIV infection**
1. Endothelial dysfunction
2. Lipid disorders associated with HIV infection
3. Viral protein-related endothelial cell activation
4. Systemic inflammatory cytokine-chemokine dysregulation
5. Direct HIV infection of endothelium and vascular smooth muscle cells
6. Enhanced atheroma formation by activated macrophages
7. Prothrombotic state

**ART**
1. Endothelial dysfunction
2. Increased endothelial permeability
3. Increased oxidative stress
4. Increased mononuclear cell adhesion
5. Insulin resistance
6. Accelerated lipid accumulation in vessel wall
7. Persistent inflammation and immune activation
8. Impaired response to vascular injury
9. ART-associated lipodystrophy leading to metabolic disorders, increased systemic inflammation, and reduced circulating adiponectin

Dubé MP et al., Circulation. 2008; 118: e36-e40
Epidemiological evidence

Figure 1. Myocardial infarction rates in HIV-infected (n = 3851) versus HIV-uninfected (n = 1,044,589) patients in a Massachusetts administrative hospital database, for 1996-2004. Adapted from Triant et al, J Clin Endocrinol Metab, 2007.
Epidemiological evidence

Table 2. Rates of AMI by HIV Status and Age Group

<table>
<thead>
<tr>
<th>Status</th>
<th>&lt;30</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
<th>80-89</th>
<th>&gt;89</th>
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<tbody>
<tr>
<td>Uninfected</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>1175</td>
<td>6783</td>
<td>21866</td>
<td>19805</td>
<td>4209</td>
<td>1120</td>
<td>148</td>
<td>3</td>
</tr>
<tr>
<td>No. of AMI events</td>
<td>0</td>
<td>10</td>
<td>164</td>
<td>218</td>
<td>66</td>
<td>36</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>AMI rates per 1000 person-years (95% CI)</td>
<td>...</td>
<td>0.3</td>
<td>1.5</td>
<td>2.2</td>
<td>3.3</td>
<td>6.7</td>
<td>21.5</td>
<td>...</td>
</tr>
<tr>
<td>HIV Infected</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>725</td>
<td>3848</td>
<td>10575</td>
<td>9342</td>
<td>2065</td>
<td>557</td>
<td>56</td>
<td>0</td>
</tr>
<tr>
<td>No. of AMI events</td>
<td>0</td>
<td>13</td>
<td>105</td>
<td>171</td>
<td>46</td>
<td>25</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>AMI rates per 1000 person-years (95% CI)</td>
<td>...</td>
<td>0.7</td>
<td>2.0</td>
<td>3.9</td>
<td>5.0</td>
<td>10.0</td>
<td>13.5</td>
<td>...</td>
</tr>
<tr>
<td>Incidence rate ratio (95% CI)</td>
<td>...</td>
<td>2.19</td>
<td>1.34</td>
<td>1.80</td>
<td>1.53</td>
<td>1.03</td>
<td>1.50</td>
<td>0.63</td>
</tr>
</tbody>
</table>

• When adjusted for Framingham Risk Factors, the overall risk of AMI was 50% higher in HIV-infected participants vs HIV-negative participants;

• NRTI’s and NNRTI’s were not associated with AMI; and protease inhibitors caused 34% increased risk (p=0.06)

Epidemiological evidence

Vascular Disease effects:

Case-control study in Germany
HIV+: n=292 vs HIV-free controls: n=1168

Effects of HAART:
• Patients on >2 years HAART: $\sim \uparrow 20\%$ Carotid IMT vs. HAART naïve (p<0.0001)
• Patients on <1 year NRTI: $\sim \uparrow 48\%$ Carotid IMT vs. NNRTI or PI (p<0.0005)
• Patients on >2 years NRTI: $\sim \uparrow 28\%$ Carotid IMT vs NNRTI or PI (p<0.0001)
Epidemiological evidence: Endothelial function in HIV-infected South Africans

Fourie CMT et al., Atherosclerosis. 2015
C-reactive protein (CRP): the golden biomarker of cardiovascular risk in HIV-infected people?

Atherosclerosis / Coronary Artery Disease

Biomarkers of Inflammation in Cardiovascular Risk Prediction
- Myeloperoxidase
- Lipoprotein-associated phospholipase A2
- IL-6 (cytokine)
- CRP (high sensitivity (hs) CRP assay)

Libby P et al., JACC 2009
C-reactive protein (CRP): the golden biomarker of cardiovascular risk in HIV-infected people?

Myeloid cells: Monocytes, Macrophages, Neutrophils etc.
AIM:

To investigate whether HIV-infection and ART are associated with vascular function, and whether hs-CRP is a biomarker of pre-clinical vascular disease in HIV.
Participant ≥ 18 years old
Participant not pregnant
Participant ≥ 3 months post-partum

**NO** to any one of the above

Exclude from study

**YES** to all of the above

HIV status

Positive

Exclude from study

Negative

Treatment status

Already on ART

No ART / ART ≤ 4 weeks

Include as HIV-positive on Rx

Include as HIV-positive (no Rx) control

Include as HIV-negative control

Informed consent, questionnaire, weight, BMI, waist-hip ratio, BP, heart rate, urine dipstix, urine sample.
Fasting blood collection, FMD and retinal camera (fasting)

Follow-Up 18 months
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Data expressed as:</th>
<th>HIV-NEGATIVE (N=97)</th>
<th>HIV-POSITIVE, ART NÄIVE (N=50)</th>
<th>HIV-POSITIVE WITH ART (N=199)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AGE:</td>
<td>Years (Mean±SD)</td>
<td>40.5 ± 11.4</td>
<td>34.98 ± 9.4</td>
<td>39.88 ± 8.6</td>
<td>0.02</td>
</tr>
<tr>
<td>SEX:</td>
<td>Males (N, %)</td>
<td>20; 20.6%</td>
<td>17; 34%</td>
<td>68; 34.2%</td>
<td>0.04</td>
</tr>
<tr>
<td>RACE:</td>
<td>Mixed Ancestry (N, %)</td>
<td>91; 95%</td>
<td>40; 80%</td>
<td>139; 70%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Risk Factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMOKE:</td>
<td>Yes (N, %)</td>
<td>58; 59.8%</td>
<td>32; 64%</td>
<td>101; 50.8%</td>
<td></td>
</tr>
<tr>
<td>ALCOHOL:</td>
<td>Yes (N, %)</td>
<td>50; 51.6%</td>
<td>29; 58%</td>
<td>90; 45%</td>
<td></td>
</tr>
<tr>
<td>CVS Meds:</td>
<td>Yes (N, %)</td>
<td>18; 18.6%</td>
<td>4; 8%</td>
<td>27; 13.6%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BMI:</td>
<td>Kg/m² (Mean±SD)</td>
<td>27.6 ± 7.6</td>
<td>23.4 ± 7.8</td>
<td>23.7 ± 6.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>WAIST:</td>
<td>cm (Median, IQR)</td>
<td>91.0 (79.0 - 106.0)</td>
<td>81.0 (71.0 - 92.0)</td>
<td>86.0 (78.0 - 96.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>WHR:</td>
<td>Mean±SD</td>
<td>0.90 ± 0.08</td>
<td>0.89 ± 0.1</td>
<td>0.90 ± 0.08</td>
<td></td>
</tr>
<tr>
<td>SBP:</td>
<td>mmHg (Mean±SD)</td>
<td>125.5 ± 19.8</td>
<td>118.0 ± 15.7</td>
<td>123.6 ± 18.9</td>
<td>0.07</td>
</tr>
<tr>
<td>DBP:</td>
<td>mmHg (Median, IQR)</td>
<td>86.3 (78.0 - 94.00)</td>
<td>82.3 (73.7 - 89.3)</td>
<td>84.0 (76.7 - 92.3)</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>Blood Chemistry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL:</td>
<td>mmol/L (Mean±SD)</td>
<td>2.5 ± 0.8</td>
<td>2.4 ± 0.8</td>
<td>2.5 ± 0.8</td>
<td></td>
</tr>
<tr>
<td>TG:</td>
<td>mmol/L (Median, IQR)</td>
<td>0.96 (0.74 - 1.48)</td>
<td>0.87 (0.59 - 1.24)</td>
<td>1.0 (0.8 - 1.4)</td>
<td>0.05</td>
</tr>
<tr>
<td>GLU:</td>
<td>mmol/L (Median, IQR)</td>
<td>4.6 (4.2 - 5.0)</td>
<td>4.4 (4.2 - 5.0)</td>
<td>4.7 (4.3 - 5.1)</td>
<td></td>
</tr>
<tr>
<td>HBA1C:</td>
<td>% (Median, IQR)</td>
<td>5.3 (5.0 - 5.6)</td>
<td>5.5 (5.0 - 5.6)</td>
<td>5.3 (5.0 - 5.6)</td>
<td></td>
</tr>
<tr>
<td>CREA:</td>
<td>μmol/L (Median, IQR)</td>
<td>61.0 (54.0 - 70.0)</td>
<td>57.6 (48.0 - 66.0)</td>
<td>57.0 (50.0 - 68.0)</td>
<td></td>
</tr>
<tr>
<td>GGT:</td>
<td>U/L (Median, IQR)</td>
<td>24.0 (17.5 - 36.5)</td>
<td>24.5 (17.0 - 34.0)</td>
<td>45.0 (30.0 - 85.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>HIV parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ART DURATION:</td>
<td>Weeks (Mean±SD)</td>
<td>n/a</td>
<td>n/a</td>
<td>216.1 ± 392.0</td>
<td></td>
</tr>
<tr>
<td>CD4:</td>
<td>Cells / μL (Mean±SD)</td>
<td>n/a</td>
<td>470.96 ± 250.0</td>
<td>492.4 ± 253.9</td>
<td></td>
</tr>
<tr>
<td>VL:</td>
<td>RNA copies/mL (Median, IQR)</td>
<td>n/a</td>
<td>13123.0 (15345.5 - 65439.5)</td>
<td>28.0 (20.0 - 324.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Inflammation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hs-CRP:</td>
<td>mg / dL (Median, IQR)</td>
<td>4.4 (1.5 - 10.2)</td>
<td>5.2 (1.0 - 15.4)</td>
<td>5.1 (1.7 - 9.7)</td>
<td></td>
</tr>
<tr>
<td>CRP RANK:</td>
<td>&gt;3mg/dL (N, %)</td>
<td>61; 62.9%</td>
<td>28; 56%</td>
<td>123; 62%</td>
<td></td>
</tr>
<tr>
<td><strong>Vascular endpoints</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DIAM CHANGE:</td>
<td>mm (Mean±SD)</td>
<td>0.211 ± 0.15</td>
<td>0.21 ± 0.2</td>
<td>0.26 ± 0.18</td>
<td>0.02</td>
</tr>
<tr>
<td>%FMD</td>
<td>Median (IQR)</td>
<td>5.58 (3.15 - 8.73)</td>
<td>5.22 (2.86 - 10.35)</td>
<td>7.26 (4.0 - 10.6)</td>
<td>0.03</td>
</tr>
<tr>
<td>%FMD RANK:</td>
<td>Dysfunction: &lt;6.52% (N, %)</td>
<td>58; 59.8%</td>
<td>29; 58%</td>
<td>84; 42.6%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRAE:</td>
<td>μM (Mean±SD)</td>
<td>153.13 ± 15.8</td>
<td>157.6 ± 16.1</td>
<td>151.8 ± 14.7</td>
<td>0.06</td>
</tr>
<tr>
<td>CRVE:</td>
<td>μM (Mean±SD)</td>
<td>234.87 ± 19.7</td>
<td>240.53 ± 26.7</td>
<td>226.5 ± 18.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AVR:</td>
<td>Mean ± SD</td>
<td>0.65 ± 0.07</td>
<td>0.66 ± 0.1</td>
<td>0.67 ± 0.06</td>
<td></td>
</tr>
</tbody>
</table>
Control Variables vs HIV-status
Age vs HIV-status; LS Means
Current effect: F(2, 342)=6.1666, p=.00234
Vertical bars denote 0.95 confidence intervals
BMI vs HIV-status; LS Means
Current effect: $F(2, 341)=11.901$, $p=0.00001$
Vertical bars denote 0.95 confidence intervals
HIV Neg vs Pos Treatment Status; LS Means
Current effect: F(2, 343)=3.0624, p=0.04806
Vertical bars denote 0.95 confidence intervals
Log GGT vs HIV status; LS Means
Current effect: F(2, 342)=31.084, p=.00000
Vertical bars denote 0.95 confidence intervals
Biomarkers of Vascular Inflammation (data from separate sub-study)
P-selectin

ICAM-1

**P-selectin**

- **HIV-Negative**
- **HIV-Positive ART Naive**
- **HIV-Positive with ART**

- **p<0.0001**
- **p=0.0018**

**ICAM-1**

- **HIV-Negative**
- **HIV-Positive ART Naive**
- **HIV-Positive with ART**

- **p=0.08**
- **p=0.04**
Control Variables vs Vascular Endpoints
SMOKE vs %FMD; LS Means

Current effect: F(1, 342)=3.7122, p=0.05 Mann-Whitney U p=0.02

Vertical bars denote 0.95 confidence intervals
SMOKE vs CRAE; LS Means
Current effect: $F(1, 331)=5.7332$, $p=0.02$ Mann-Whitney $U$ $p=0.03$
Vertical bars denote 0.95 confidence intervals
SMOKE vs CRVE; LS Means
Current effect: F(1, 331)=14.579, p=<0.01 Mann-Whitney U p<0.01
Vertical bars denote 0.95 confidence intervals
ALCOHOL vs %FMD; LS Means
Current effect: F(1, 342)=5.5852, p=0.02 Mann-Whitney U p<0.01
Vertical bars denote 0.95 confidence intervals
<table>
<thead>
<tr>
<th>Vascular Endpoint</th>
<th>Control Variable</th>
<th>Pearson's r</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>%FMD</td>
<td>log CREA</td>
<td>-0.11</td>
<td>0.03</td>
</tr>
<tr>
<td>%FMD</td>
<td>AGE</td>
<td>-0.11</td>
<td>0.04</td>
</tr>
<tr>
<td>CRAE</td>
<td>AGE</td>
<td>-0.19</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRAE</td>
<td>DBP</td>
<td>-0.41</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRAE</td>
<td>log GGT</td>
<td>-0.15</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRAE</td>
<td>log WAIST</td>
<td>-0.14</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRAE</td>
<td>SBP</td>
<td>-0.29</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRAE</td>
<td>WHR</td>
<td>-0.20</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRAE</td>
<td>log TG</td>
<td>-0.14</td>
<td>0.01</td>
</tr>
<tr>
<td>CRAE</td>
<td>log CREA</td>
<td>-0.12</td>
<td>0.03</td>
</tr>
<tr>
<td>CRVE</td>
<td>DBP</td>
<td>-0.19</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRVE</td>
<td>WHR</td>
<td>-0.17</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRVE</td>
<td>log CREA</td>
<td>-0.13</td>
<td>0.01</td>
</tr>
<tr>
<td>CRVE</td>
<td>log GGT</td>
<td>-0.12</td>
<td>0.03</td>
</tr>
<tr>
<td>CRVE</td>
<td>log WAIST</td>
<td>-0.12</td>
<td>0.04</td>
</tr>
<tr>
<td>AVR</td>
<td>DBP</td>
<td>-0.25</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AVR</td>
<td>SBP</td>
<td>-0.19</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AVR</td>
<td>log TG</td>
<td>-0.11</td>
<td>0.04</td>
</tr>
</tbody>
</table>
Adjusting for covariates
%FMD vs HIV-status; LS Means
Current effect: $F(2, 331)=3.8454, p=0.02234$
Vertical bars denote 0.95 confidence intervals

*: $p=0.02$ vs HIV-Neg
CRVE vs HIV-Status

F(2,312)=8.501, p<0.01

Vertical bars denote 0.95 confidence intervals

Adjusted for: log Waist, WHR, SBP, DBP, log Crea, log HbA1C, log GGT, Race, Smoke

*: p<0.01 vs Pos with ART
Associations with vascular endpoints
### Whole Cohort: HIV- and HIV+

**Dependent Variable: %FMD**

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Level</th>
<th>t</th>
<th>p-value</th>
<th>β</th>
<th>Std Error β</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td></td>
<td>-2.15960</td>
<td>0.031517</td>
<td>-0.118887</td>
<td>0.055051</td>
<td>-0.227179 to -0.010596</td>
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<tr>
<td>log DBP</td>
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<td>0.84852</td>
<td>0.396760</td>
<td>0.046835</td>
<td>0.055196</td>
<td>-0.061743 to 0.155413</td>
</tr>
<tr>
<td>log CREA</td>
<td></td>
<td>-1.62631</td>
<td>0.104830</td>
<td>-0.087481</td>
<td>0.053791</td>
<td>-0.193293 to 0.018332</td>
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<tr>
<td>SMOKE</td>
<td>no</td>
<td>1.59772</td>
<td>0.111054</td>
<td>0.087533</td>
<td>0.054786</td>
<td>-0.020238 to 0.195303</td>
</tr>
<tr>
<td>ALCOHOL</td>
<td>no</td>
<td>1.89686</td>
<td><strong>0.058711</strong></td>
<td>0.102979</td>
<td>0.054289</td>
<td>-0.003814 to 0.209773</td>
</tr>
<tr>
<td>HIV Neg vs Pos</td>
<td>neg</td>
<td>-1.77941</td>
<td><strong>0.076084</strong></td>
<td>-0.095881</td>
<td>0.053883</td>
<td>-0.201875 to 0.010114</td>
</tr>
</tbody>
</table>

*Adjusted R²: 0.06; F: 3.40; p=0.003*

### HIV+ group

**Dependent Variable: %FMD**

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Level</th>
<th>t</th>
<th>p-value</th>
<th>β</th>
<th>Std Error β</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td></td>
<td>-1.94183</td>
<td><strong>0.053337</strong></td>
<td>-0.128428</td>
<td>0.066137</td>
<td>-0.258718 to 0.001862</td>
</tr>
<tr>
<td>log DBP</td>
<td></td>
<td>0.44147</td>
<td>0.659275</td>
<td>0.028827</td>
<td>0.065297</td>
<td>-0.099807 to 0.157461</td>
</tr>
<tr>
<td>log CREA</td>
<td></td>
<td>-0.96699</td>
<td>0.334532</td>
<td>-0.061530</td>
<td>0.063631</td>
<td>-0.186882 to 0.063821</td>
</tr>
<tr>
<td>HIV-Pos</td>
<td>No ART</td>
<td><strong>2.02963</strong></td>
<td><strong>0.043507</strong></td>
<td><strong>-0.132812</strong></td>
<td><strong>0.065437</strong></td>
<td><strong>-0.261722 to -0.003903</strong></td>
</tr>
<tr>
<td>SMOKE</td>
<td>no</td>
<td>1.44198</td>
<td>0.150622</td>
<td>0.093503</td>
<td>0.064843</td>
<td>-0.034237 to 0.221243</td>
</tr>
<tr>
<td>ALCOHOL</td>
<td>no</td>
<td>1.05365</td>
<td>0.293114</td>
<td>0.067660</td>
<td>0.064215</td>
<td>-0.058843 to 0.194162</td>
</tr>
</tbody>
</table>

*Adjusted R²: 0.03; F: 2.18; p=0.04*
### Whole Cohort: HIV- and HIV+

**Dependent Variable: CRVE**

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Level</th>
<th>t</th>
<th>p-value</th>
<th>( \beta )</th>
<th>Std Error ( \beta )</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Neg vs Pos</td>
<td></td>
<td>-1.68464</td>
<td>0.093046</td>
<td>-0.098830</td>
<td>0.058665</td>
<td>-0.214254 to 0.016594</td>
</tr>
<tr>
<td>AGE</td>
<td></td>
<td>-0.09426</td>
<td>0.924960</td>
<td>-0.005279</td>
<td>0.056000</td>
<td>-0.115458 to 0.104900</td>
</tr>
<tr>
<td>log WAIST</td>
<td></td>
<td>-0.39949</td>
<td>0.689803</td>
<td>-0.024221</td>
<td>0.060630</td>
<td>-0.143510 to 0.095068</td>
</tr>
<tr>
<td>log DBP</td>
<td></td>
<td>-3.67390</td>
<td>0.000280</td>
<td>-0.205490</td>
<td>0.055932</td>
<td>-0.315537 to -0.095443</td>
</tr>
<tr>
<td>log CREA</td>
<td></td>
<td>-2.48277</td>
<td>0.013555</td>
<td>-0.134186</td>
<td>0.054047</td>
<td>-0.240523 to -0.027849</td>
</tr>
<tr>
<td>log GGT</td>
<td></td>
<td>-0.70642</td>
<td>0.480450</td>
<td>-0.040230</td>
<td>0.056949</td>
<td>-0.152277 to 0.071817</td>
</tr>
<tr>
<td>RACE</td>
<td>black</td>
<td>-0.86743</td>
<td>0.386365</td>
<td>-0.050485</td>
<td>0.058201</td>
<td>-0.164996 to 0.064025</td>
</tr>
<tr>
<td>SMOKE</td>
<td>no</td>
<td>-2.59394</td>
<td>0.009930</td>
<td>-0.155467</td>
<td>0.059935</td>
<td>-0.273389 to -0.037546</td>
</tr>
</tbody>
</table>

Adjusted \( R^2 \): 0.1; F: 5.43; p<0.01

### HIV+ Group

**Dependent Variable: CRVE**

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Level</th>
<th>t</th>
<th>p-value</th>
<th>( \beta )</th>
<th>Std Error ( \beta )</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td></td>
<td>0.21695</td>
<td>0.828441</td>
<td>0.014004</td>
<td>0.064550</td>
<td>-0.113190 to 0.141199</td>
</tr>
<tr>
<td>log WAIST</td>
<td></td>
<td>-2.00189</td>
<td>0.046487</td>
<td>-0.134964</td>
<td>0.067418</td>
<td>-0.267809 to -0.002118</td>
</tr>
<tr>
<td>log DBP</td>
<td></td>
<td>-2.93535</td>
<td>0.003674</td>
<td>-0.186175</td>
<td>0.063425</td>
<td>-0.311151 to -0.061198</td>
</tr>
<tr>
<td>log CREA</td>
<td></td>
<td>-2.63755</td>
<td>0.008928</td>
<td>-0.161722</td>
<td>0.061315</td>
<td>-0.282542 to -0.040902</td>
</tr>
<tr>
<td>log GGT</td>
<td></td>
<td>0.74089</td>
<td>0.459524</td>
<td>0.049146</td>
<td>0.066333</td>
<td>-0.081561 to 0.179853</td>
</tr>
<tr>
<td>HIV-Pos</td>
<td>No ART</td>
<td>3.57563</td>
<td>0.000427</td>
<td>0.232659</td>
<td>0.065068</td>
<td>0.104445 to 0.360874</td>
</tr>
<tr>
<td>RACE</td>
<td>black</td>
<td>-0.85649</td>
<td>0.392629</td>
<td>-0.055198</td>
<td>0.064447</td>
<td>-0.182188 to 0.071792</td>
</tr>
<tr>
<td>SMOKE</td>
<td>no</td>
<td>-1.32584</td>
<td>0.186226</td>
<td>-0.090955</td>
<td>0.068602</td>
<td>-0.226133 to 0.044223</td>
</tr>
</tbody>
</table>

Adjusted \( R^2 \): 0.16; F: 6.63; p<0.01
Odds Ratios for normal endothelial function (FMD>6.5%) in the whole cohort (HIV-Neg and HIV-Pos)

Reduced probability of normal function  Increased probability of normal function

Alcohol (No)  
1.46 (0.93 -2.29); p=0.09

Smoke (No)  
1.7 (1.07 - 2.68); p=0.02

HIV-Neg  
0.59 (0.36 - 0.97); p=0.03

Log Creat  
0.22 (0.02 - 2.29); p=0.20

Age  
0.97 (0.95 - 0.99); p=0.01
Odds Ratios for normal endothelial function (FMD > 6.5%) in the HIV-Pos Group

Reduced probability of normal function

- Alcohol (No)
  - 1.55 (0.92 – 2.63); p = 0.10

- Smoke (No)
  - 1.9 (1.12 – 3.2); p = 0.01

- HIV-Positive ART Naïve
  - 0.52 (0.26 – 1.0); p = 0.05

- Log Creat
  - 0.53 (0.04 – 8.1); p = 0.65

Increased probability of normal function

- Age
  - 0.97 (0.94 – 1.0); p = 0.04
Associations of hs-CRP with Vascular Endpoints?

Adjusted for:
- Log Waist, WHR, SBP, DBP, log Crea, log HBA1C,
- log GGT, Race, Smoke

CRVE vs CRP RANK

$F(1,313)=3.791, p=0.05$

Vertical bars denote 0.95 confidence intervals
Summary of the cardiovascular and vascular characteristics of our HIV cohort

**DEMOGRAPHICS:** \(\uparrow\) Chance to be younger (if untreated), male and black

**MODIFIABLE RISK FACTORS:** \(\downarrow\) Chance to be overweight and centrally obese, \(\uparrow\) chance to have lower BP, but same smoking and drinking habits

**VASCULAR FUNCTION:** 
\(\downarrow\) Risk of endothelial dysfunction (if treated), \(\uparrow\) chance of having greater endothelium-dependent vasodilation (if treated), and \(\uparrow\) chance of narrower retinal venules (if treated).

**INFLAMMATION:** 
Systemic inflammation (hs-CRP) unchanged, but signs of \(\uparrow\) vascular inflammation which improves with treatment.

**BLOOD CHEMISTRY:** 
Lipid profile and kidney function unchanged, \(\uparrow\) chance to have hepatocellular damage if treated.
• ART exerts beneficial effects on the vascular and endothelial function in HIV+ participants;
• ART is an independent, positive predictor of endothelium-dependent vascular function compared to no ART, and a negative predictor of retinal venular caliber;
• Being HIV-infected and not on ART carries a 48% decreased probability of having normal vascular endothelial function;

hs-CRP is not a biomarker of abnormal vascular function in either HIV-negative or HIV-positive participants in this cohort.
THANK YOU!