



Sex Differences in Subclinical Coronary Atherosclerotic Plaque Among Individuals with HIV on Antiretroviral Therapy

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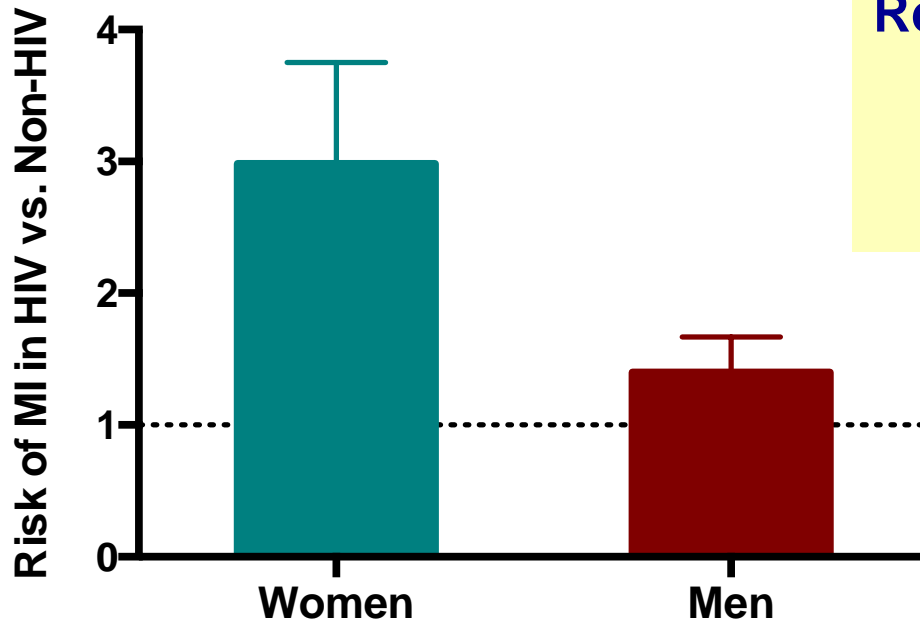
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Disclosures

- The speaker has nothing to disclose
- S.E.L.
 - Non-paid board member of the community non-profit organization Healing Our Community Collaborative
- J.L.
 - Medical Affairs Advisory Board for Gilead Sciences
 - Study drug donation from Shire for an NIH-funded study
- M.V.Z.
 - Scientific Advisory Board Meeting for Roche Diagnostics
 - Research funding to her institution for an investigator-initiated study from Gilead

Background

Women with HIV are at particularly high risk for myocardial infarction (MI)



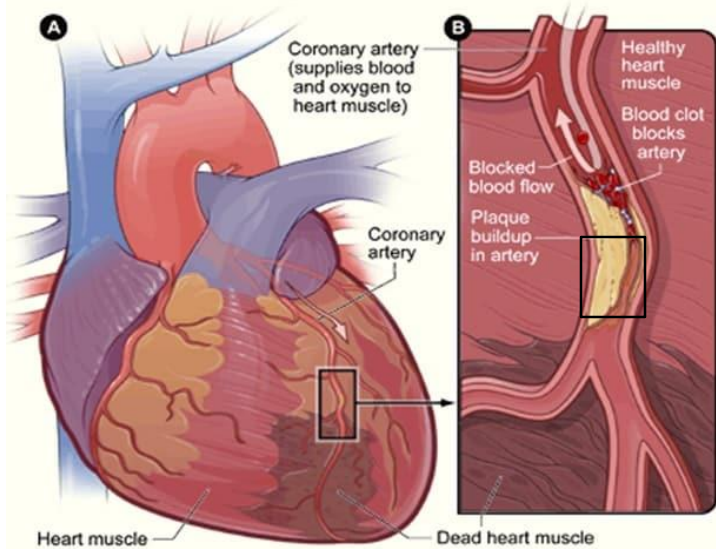
Relative Risk of MI in HIV vs. Non-HIV

Women	2.98 (2.33, 3.75)
Men	1.40 (1.16, 1.67)

Bars show mean, error bars show 95% CI

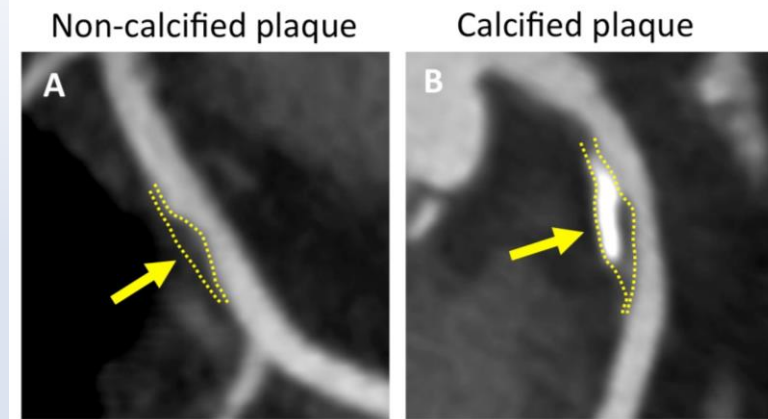
Background

A Major Mechanism of MI: Acute Plaque Rupture

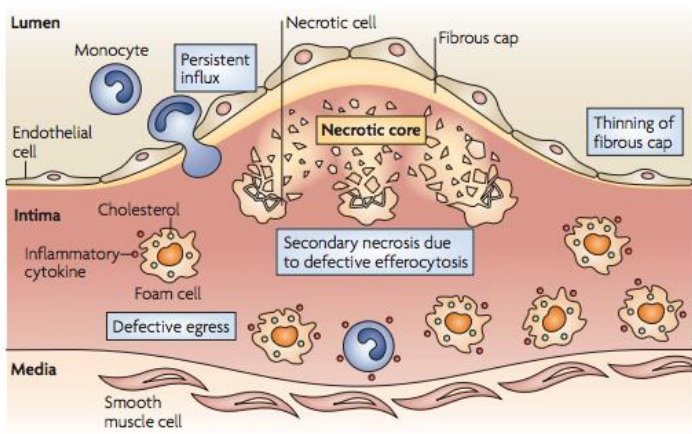
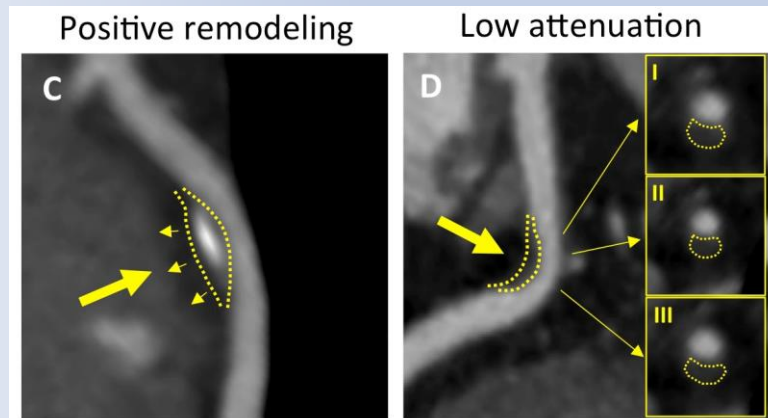


Coronary Computed Tomography Angiography (CTA) Can Distinguish Features Predictive of Plaque Rupture

Composition



High-Risk Morphology



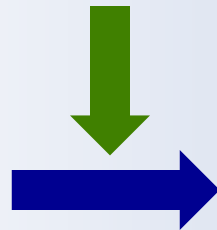
Central Objective

While women and men with HIV have similar *rates* of MI, are the *mechanisms* underlying MI similar between sexes?

Here, we utilize coronary CTA to compare the *prevalence and burden of coronary plaque and high-risk morphology plaque* between women and men with HIV and no known cardiac disease.

Sex-Specific Mechanisms of MI

~~Similar Plaque
Phenotype~~



Similar MI Rates in
Women vs. Men with HIV

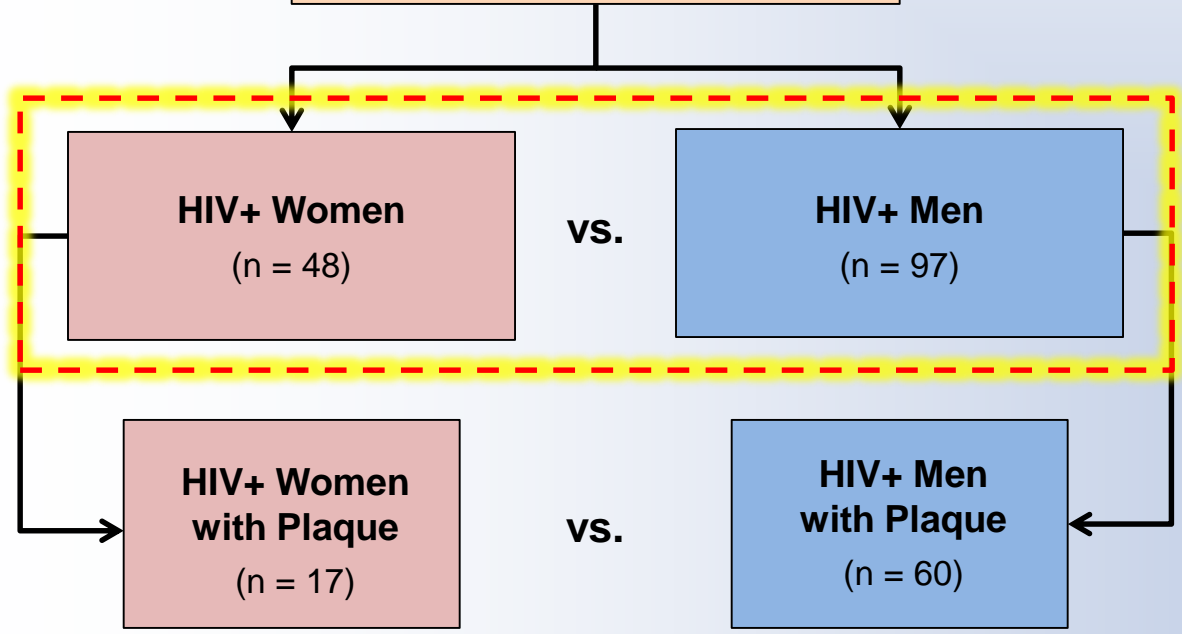
Study Design

**HIV+ women and men,
18-60 years old,
Stable ART (> 3 months),
No known CVD**

- Coronary computed tomography angiography (CTA)
- Detailed metabolic and immune phenotyping

Major Endpoints
Presence and burden of:

- Any plaque
- Non-calcified or calcified plaque
- High-risk morphology plaque features
- Obstructive plaque



Demographics and Traditional Cardiovascular Disease Risk Factors

	HIV+ Women (n = 48)	HIV+ Men (n = 97)	P-value
Age, y (median [IQR])	48 [41, 54]	48 [42, 52]	0.75
Race/Ethnicity, %			< 0.0001
White	25	65	
Black/African American	60	21	
Hispanic	8	10	
Current hypertension, %	13	27	0.04
Current diabetes, %	19	7	0.05
Current smoking, %	50	40	0.24
History of IVDU, %	25	20	0.46
History of cocaine use, %	56	71	0.08
Current statin use, %	10	17	0.28

Overall Sample

Traditional Cardiovascular Disease Risk Factors

	HIV+ Women (n = 48)	HIV+ Men (n = 97)	P-value
Total cholesterol, mg/dL	181 [156, 210]	175 [155, 203]	0.35
LDL-C, mg/dL	105 ± 37	101 ± 31	0.51
HDL-C, mg/dL	57 [44, 72]	45 [38, 55]	0.0001
Hemoglobin A1c, %	5.6 [5.4, 5.8]	5.3 [5.0, 5.7]	0.0005
BMI, kg/m ²	27.5 ± 5.2	26.2 ± 4.6	0.17
Visceral fat, cm ²	75 [34, 119]	138 [80, 258]	< 0.0001
Subcutaneous fat, cm ²	278 [195, 406]	166 [103, 233]	< 0.0001
sCD163, ng/mL	1509 [1084, 2457]	1062 [693, 1548]	0.0003
sCD14, ng/mL	2023 [1312, 2661]	307 [157, 443]	< 0.0001

Mean ± SD for normally distributed continuous variables, median [IQR] for non-normally distributed continuous variables

Overall Sample

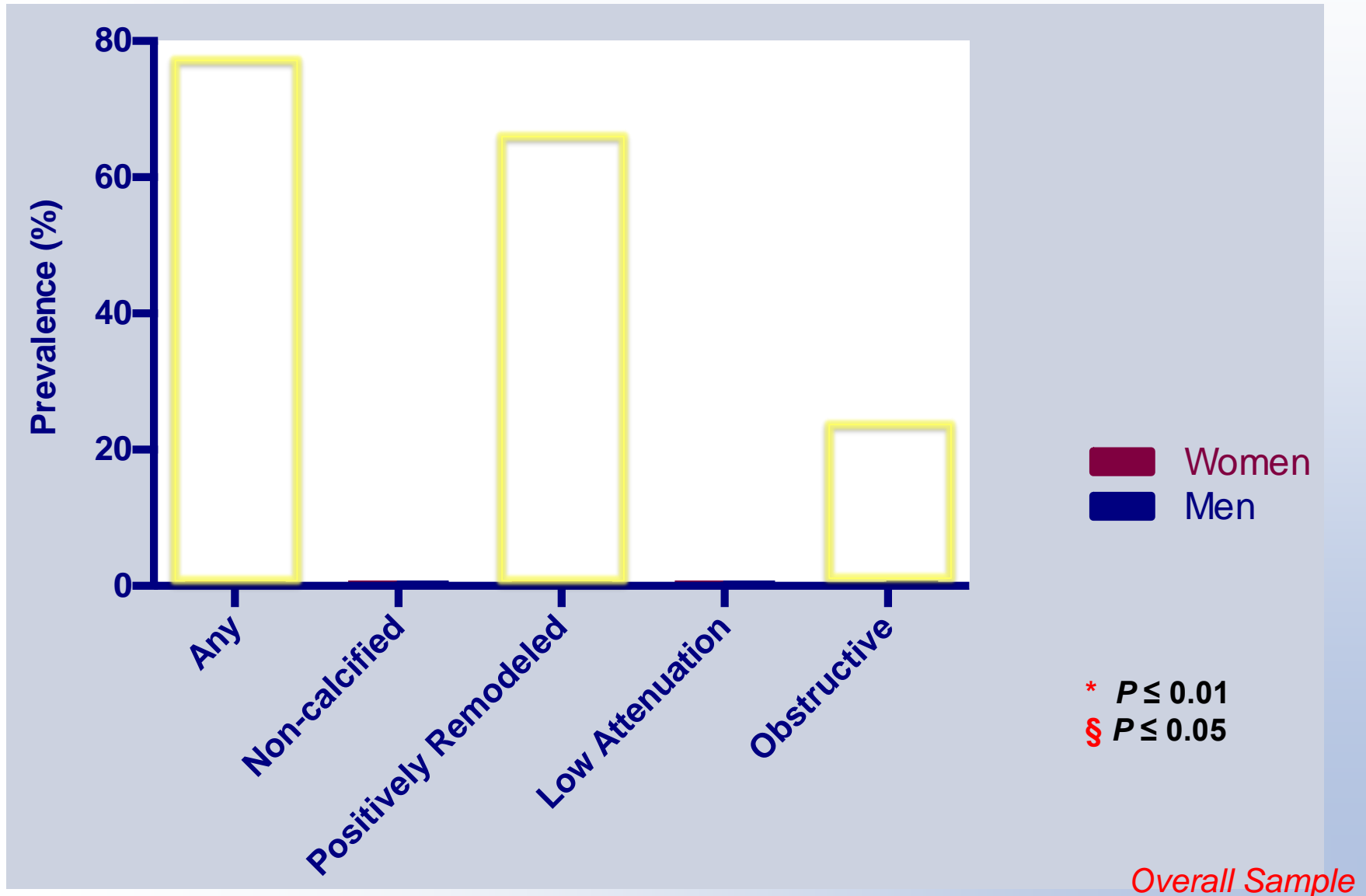
HIV-Related Parameters

	HIV+ Women (n = 48)	HIV+ Men (n = 97)	P-value
Time since diagnosis, y	14.6 ± 5.9	13.8 ± 6.5	0.46
CD4 ⁺ T cell count, cells/mm ³	535 [411, 759]	462 [303, 744]	0.10
Viral load undetectable, %	84	85	0.83
Hepatitis C co-infection, %	29	23	0.40
Total duration ART, y	8.9 [3.9, 11.8]	8.0 [4.5, 11.0]	0.51
NRTI use, %	94	97	0.38
NNRTI use, %	17	49	< 0.0001
PI use, %	63	55	0.37

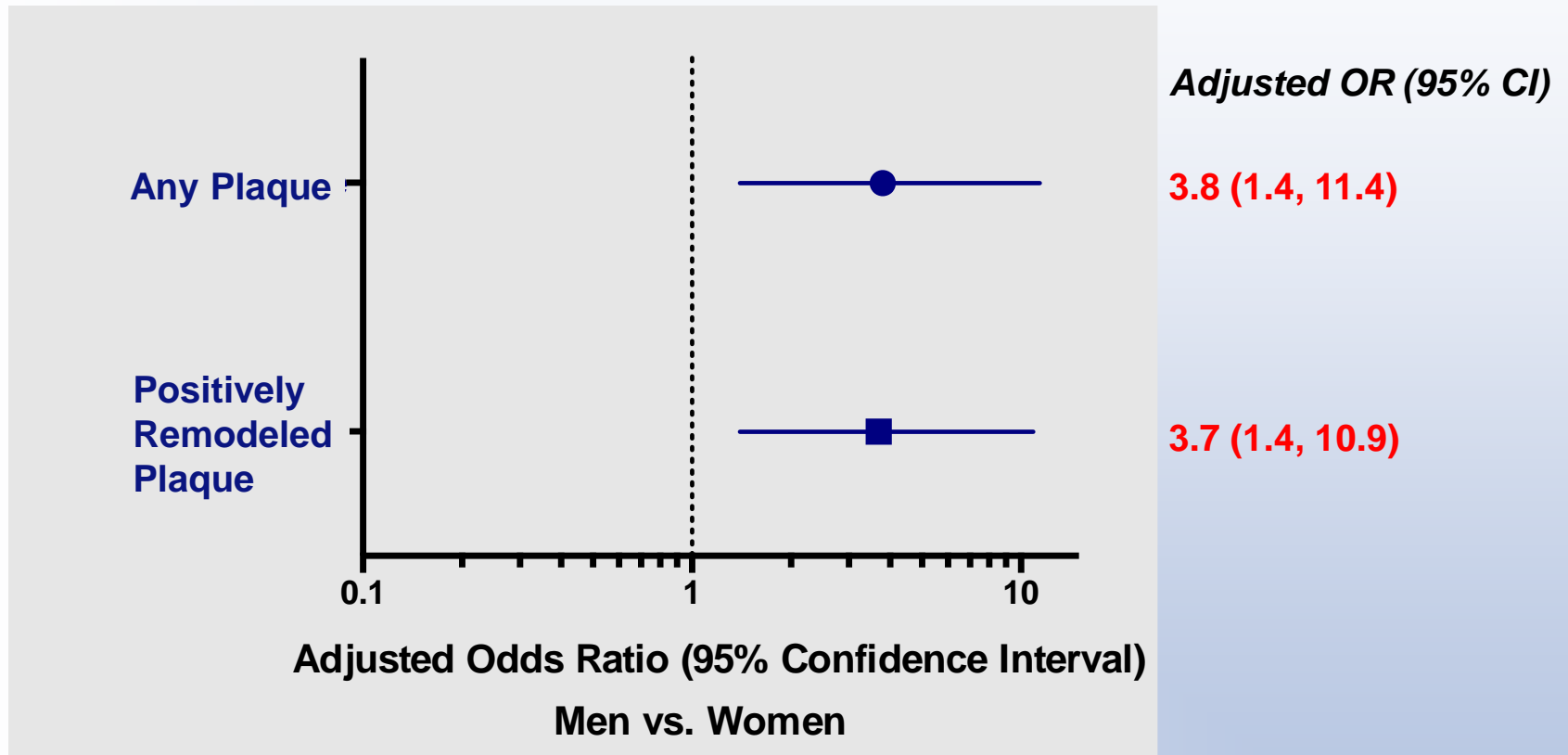
Mean ± SD for normally distributed continuous variables, median [IQR] for non-normally distributed continuous variables

Overall Sample

Sex Differences in Coronary Plaque Prevalence



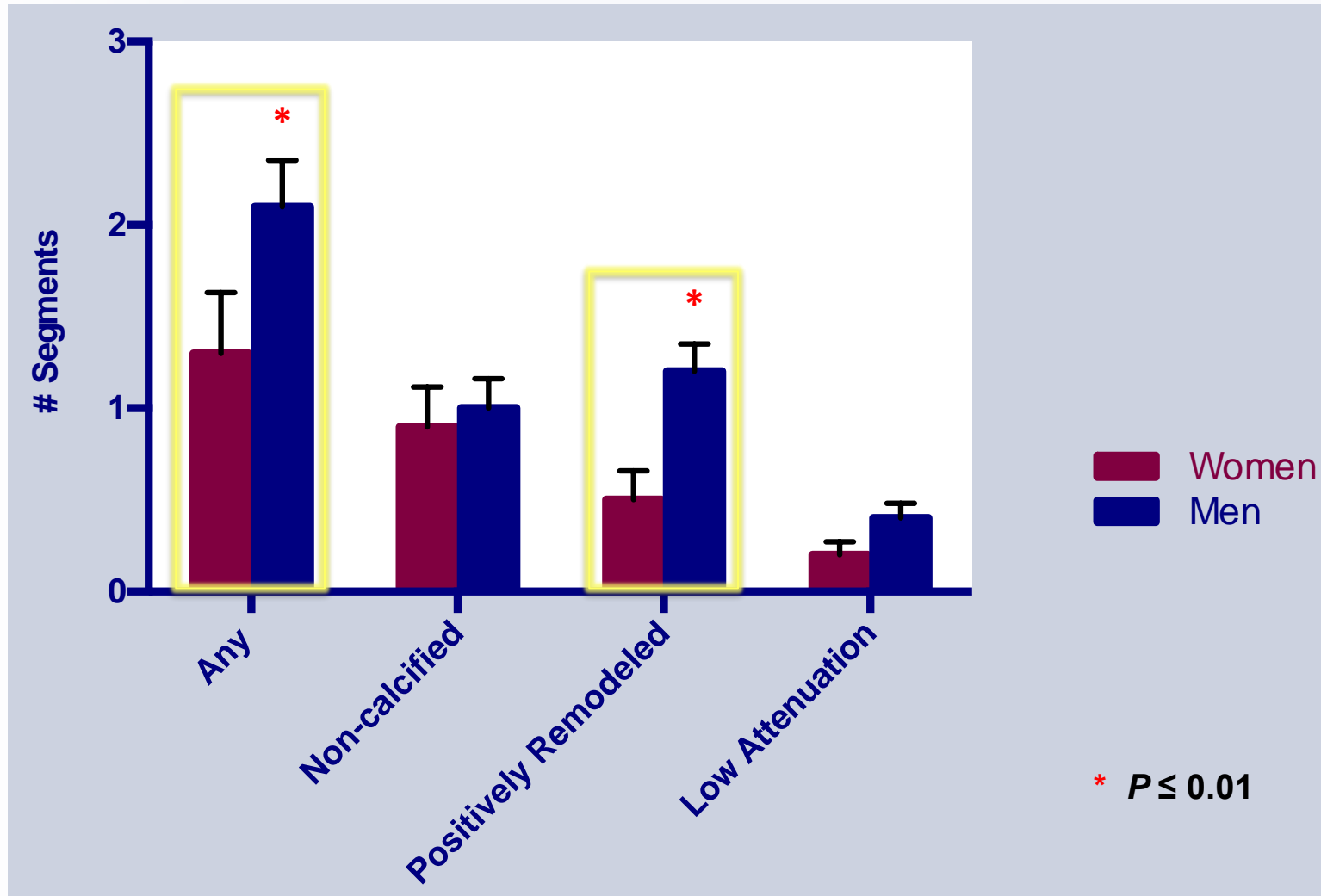
Sex Independently Predicts Coronary Plaque



Odds ratios adjusted for age, race, hypertension, diabetes, HDL-C, visceral fat, ART regimen

Overall Sample

Sex Differences in Coronary Plaque Burden



Bars show mean, error bars show SD

Overall Sample

Summary – Overall Sample

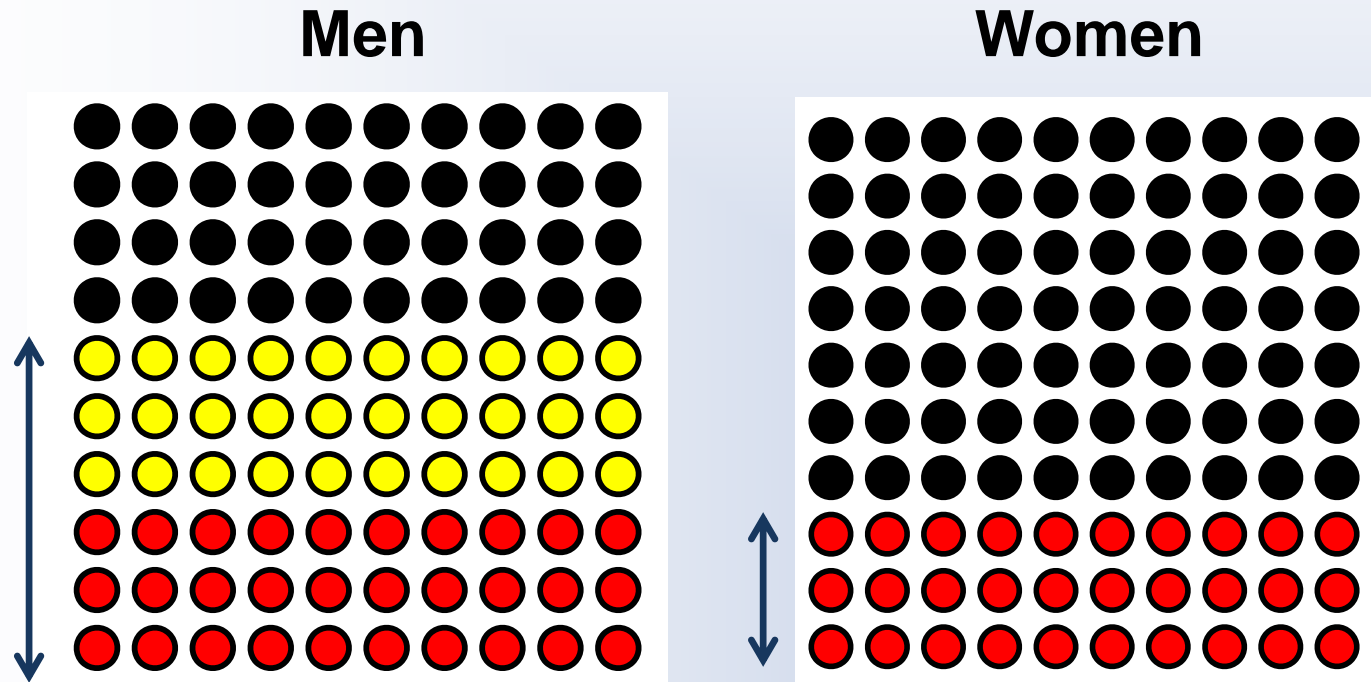
Despite comparable rates of MI in women and men with HIV, HIV-infected ART-treated women had **a lower prevalence and burden** of any plaque and of positively remodeled plaque compared to men.



Among the subset of individuals with plaque, is the phenotype more severe in women versus men?

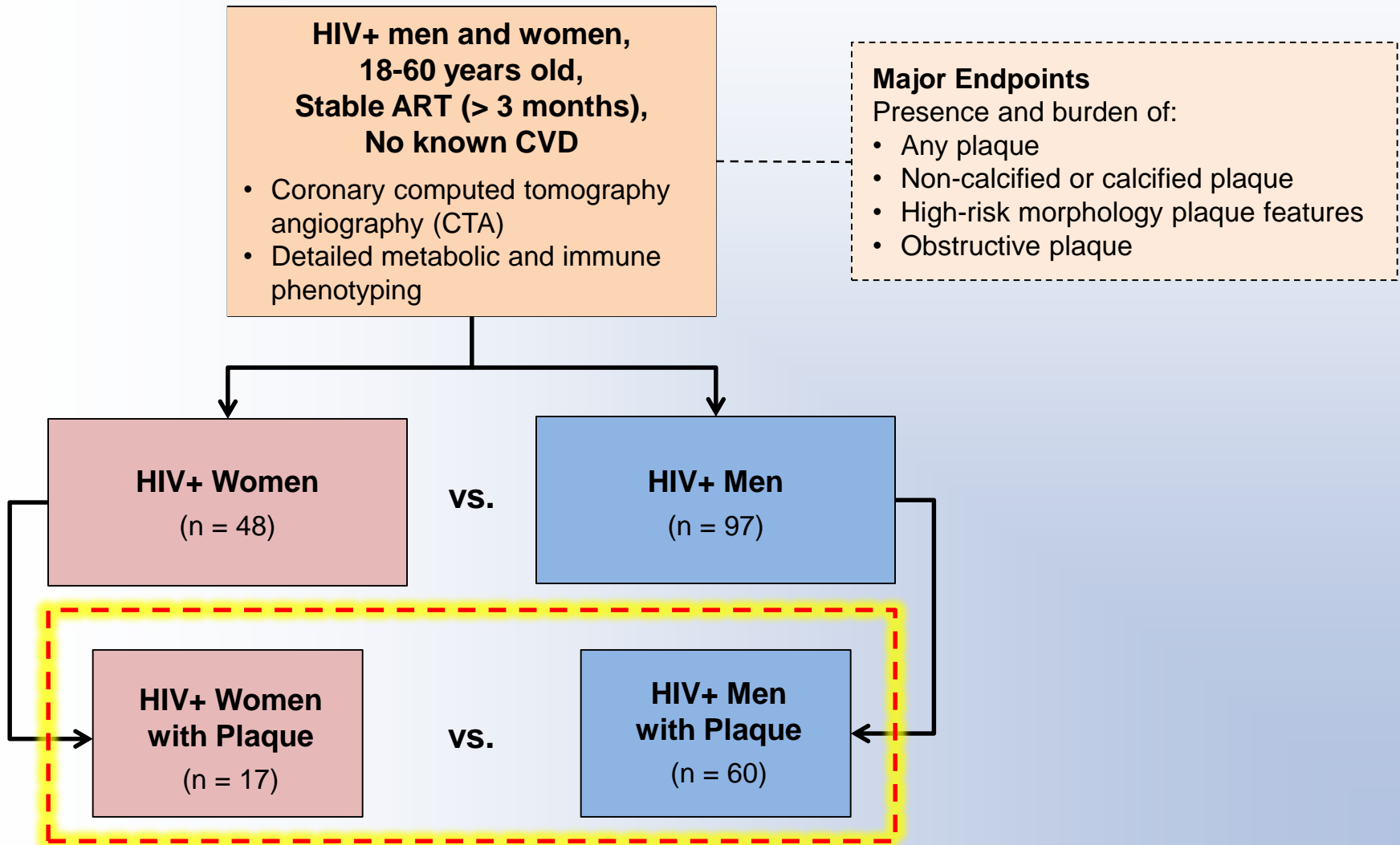
Hypothetical Scenario

Among the subset of individuals with plaque, is the phenotype more severe in women versus men?



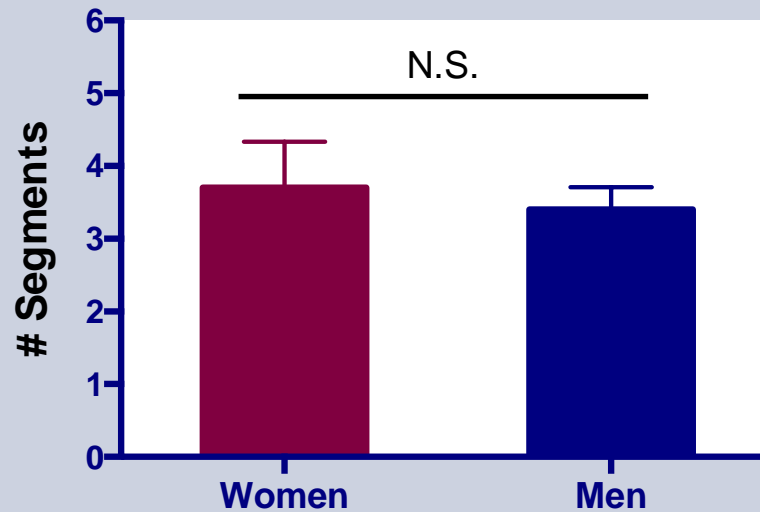
■ No plaque ■ Plaque, no rupture ■ Plaque, rupture

Study Design



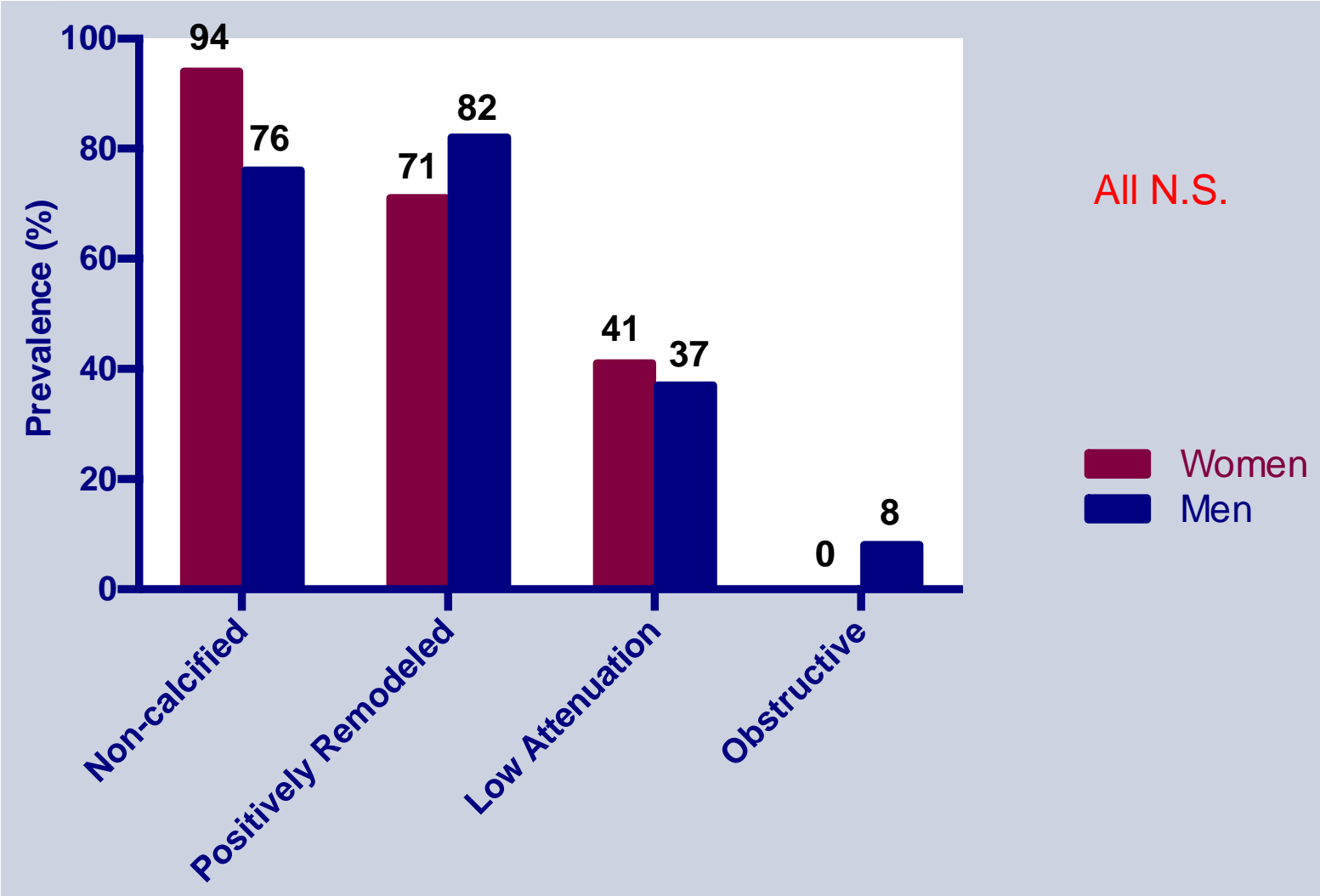
No Sex Difference in Total Plaque Segments

Total Number of Coronary Segments with Plaque



Bars show mean, error bars show SEM

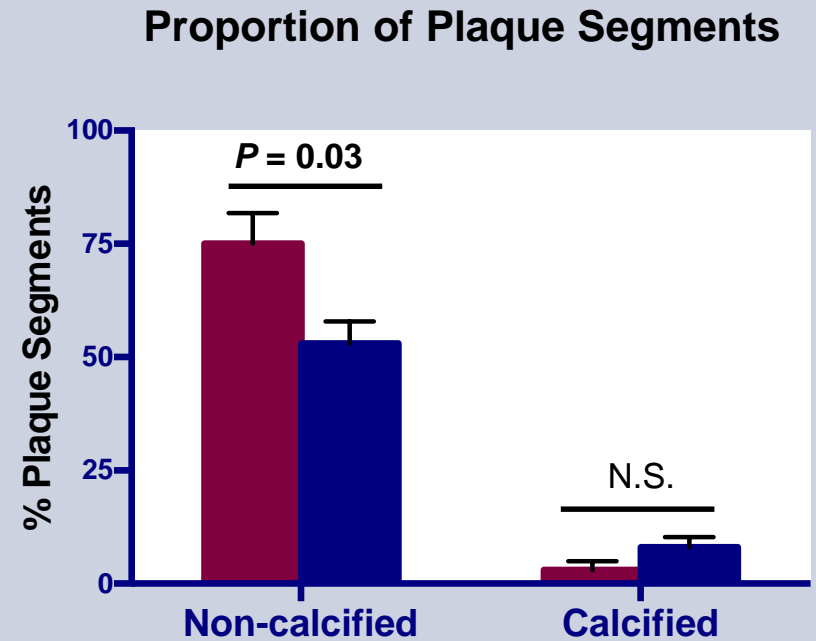
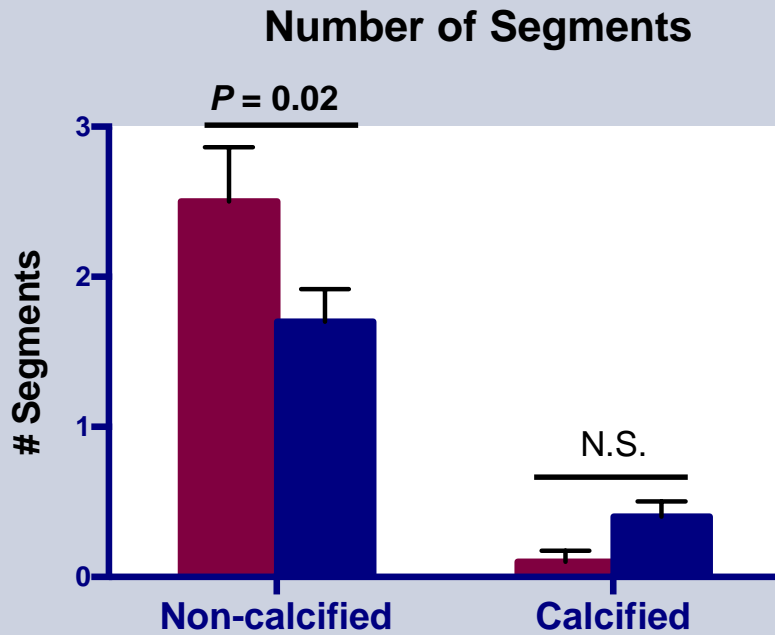
No Sex Differences in Coronary Plaque Prevalence



Individuals with Plaque

Sex Differences in Plaque Composition

Non-calcified and Calcified Plaque



■ Women ■ Men

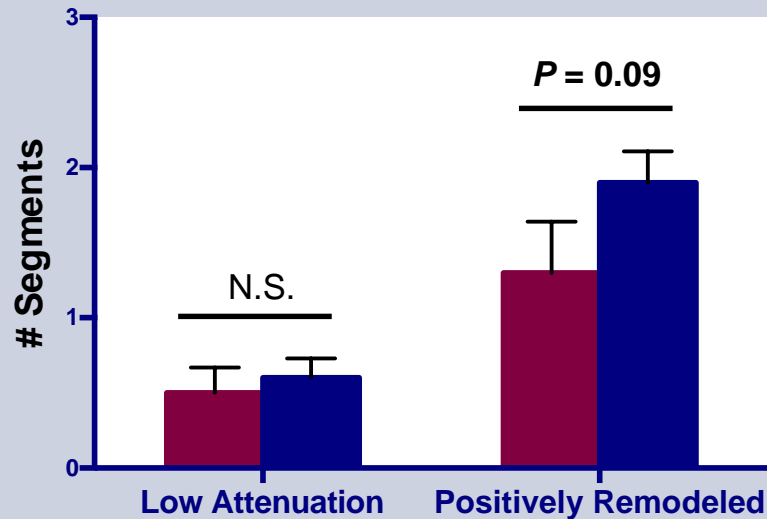
Bars show mean, error bars show SEM

Individuals with Plaque

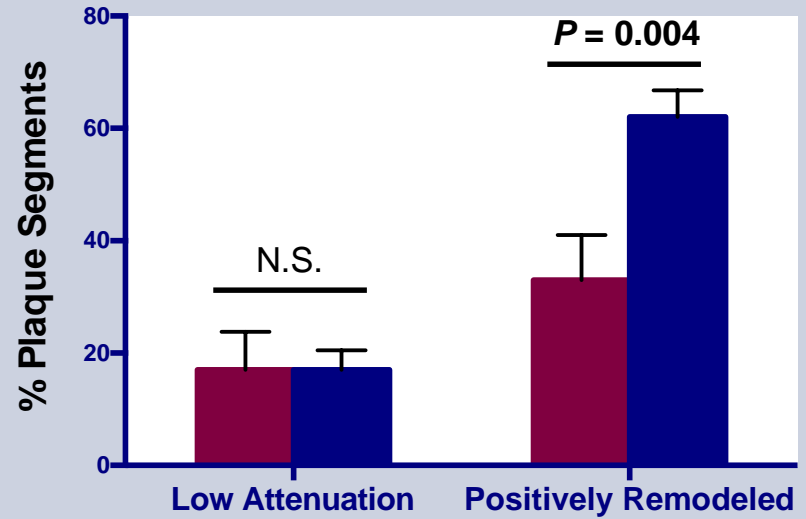
Sex Differences in Plaque High-Risk Morphology

Low Attenuation and Positive Remodeling

Number of Segments



Proportion of Plaque Segments



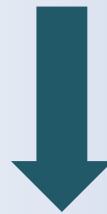
■ Women ■ Men

Bars show mean, error bars show SEM

Individuals with Plaque

Summary – Individuals with Plaque

- Compared to men, HIV-infected ART-treated **women with coronary plaque** have
 - No difference in number of affected segments or prevalence of high-risk morphology features
 - Higher burden of non-calcified plaque
 - Lower burden of positively remodeled plaque



While the absence of macroscopic plaque among women with HIV may not necessarily be reassuring, the presence of plaque in this group could be particularly worrisome

Clinical Implications

- Despite the similar rates of MI in women and men with HIV, in an analysis of asymptomatic individuals on ART, women had a **lower prevalence and burden** of coronary plaque and high-risk morphology plaque compared to men
- Mechanisms **beyond macroscopic plaque rupture** may underlie MI in women
- Only by further elucidating the mechanisms of MI among women with HIV can we appropriately tailor cardiovascular disease prevention and management to this population

Limitations

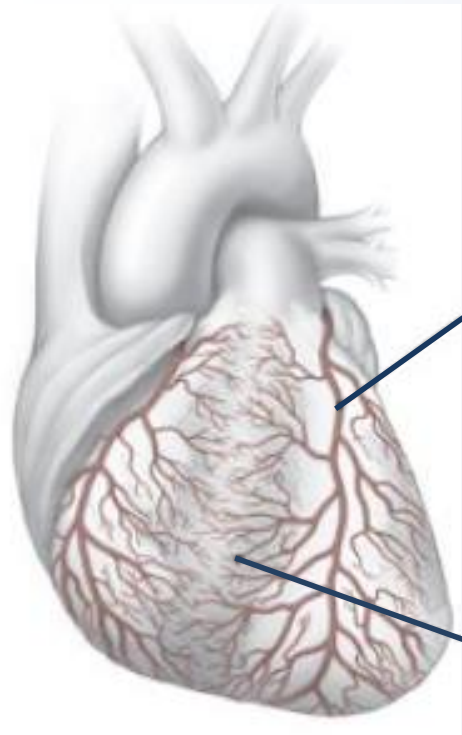
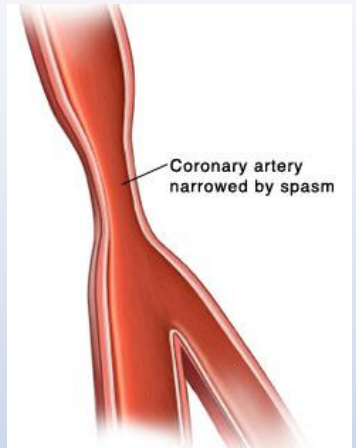
- Relatively small sample size
- Men and women were not explicitly matched
- By design, individuals with MI or angina symptoms were not assessed

Future Directions: Potential Mechanisms of MI in Women with HIV

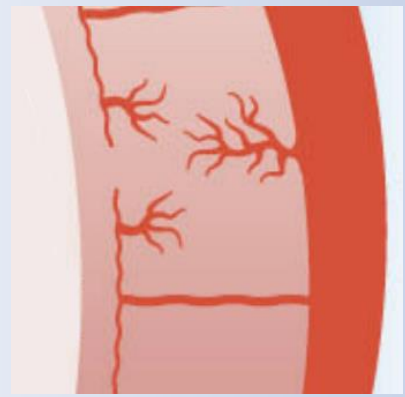
Coronary plaque erosion



Coronary vasospasm



Microvascular disease



Acknowledgements

Study participants and Nursing Staff of the MGH and MIT Clinical Research Centers

MGH Program in Nutritional Metabolism

Lauren Stone, A.B.

Janet Lo, M.D.

Mabel Toribio, M.D.

Kathleen Fitch, M.S.N.

Suman Srinivasa, M.D.

Markella Zanni, M.D.

Sara Looby, Ph.D.

Steven Grinspoon, M.D.

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