



Risk for Cardiovascular Disease and Regional Adipose Tissue Depots Among HIV-infected Men and Women in the Study of Fat Redistribution and Metabolic Changes in HIV Infection (FRAM)

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Background

- Several large observational studies suggest HIV+ patients are at heightened risk of CVD.
- The contribution of regional adipose tissue depots to CVD risk among HIV-infected patients remains unclear. A number of studies have demonstrated an association between dyslipidemia and both lipoatrophy and lipoaccumulation but these have been small and limited to selected cohorts.
- We examined the relationship between regional fat distribution and lipoprotein levels, diabetes and 10-year CVD Framingham Risk Score among participants in the FRAM study, a representative cohort of patients under care in the US, and the CARDIA study of CVD risk in the general population.

Methods

Populations:

- HIV+men and women were recruited from 16 geographically diverse HIV/ID clinics or cohorts.
- Control men and women were participants in the Coronary Artery Risk Development in Young Adults (CARDIA) study enrolled from 2 research clinics located at Kaiser Permanente, Oakland, CA and University of Alabama, Birmingham.

Evaluations:

- Whole-body MRI for regional fat volumes
- Cholesterol subsets including fasting (>8h) direct LDL-c, HDL-c and triglycerides
- Fasting blood glucose
- 10-year CVD Framingham Risk Score

Statistical Considerations:

- Characteristics of HIV-infected participants and controls were compared and tested for statistical significance using the Mann-Whitney U test for continuous variables, and Fisher's exact test for categorical variables.
- Quartiled versions of the adipose tissue depots were created using cut offs from the control group (men and women were done separately) to facilitate comparison of similar quantities of adipose tissue.
- Associations of quartiled-depots with metabolic outcomes were tested using the Jonckheere-Terpstra and Cochran-Armitage trend tests for continuous and dichotomous outcomes respectively. HIV and Control were also compared using tests of interaction between HIV status and quartiled-depot.
- Unless otherwise specified, data from HIV+ men and women are pooled in the presented analyses

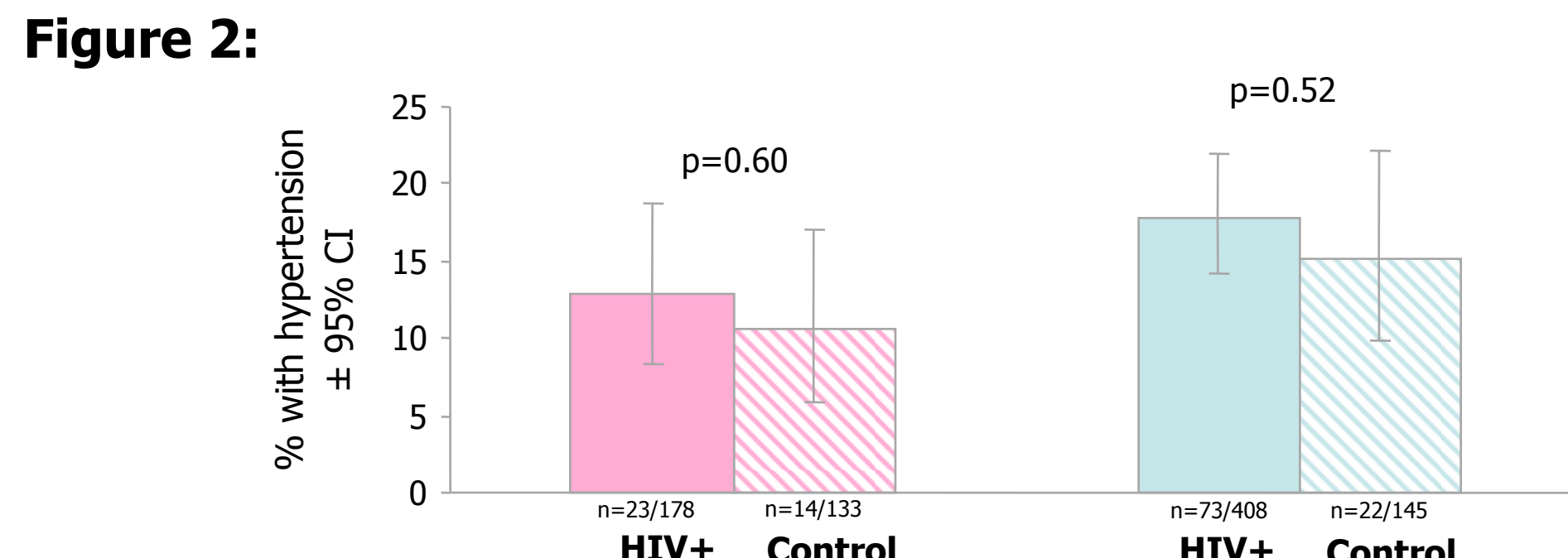
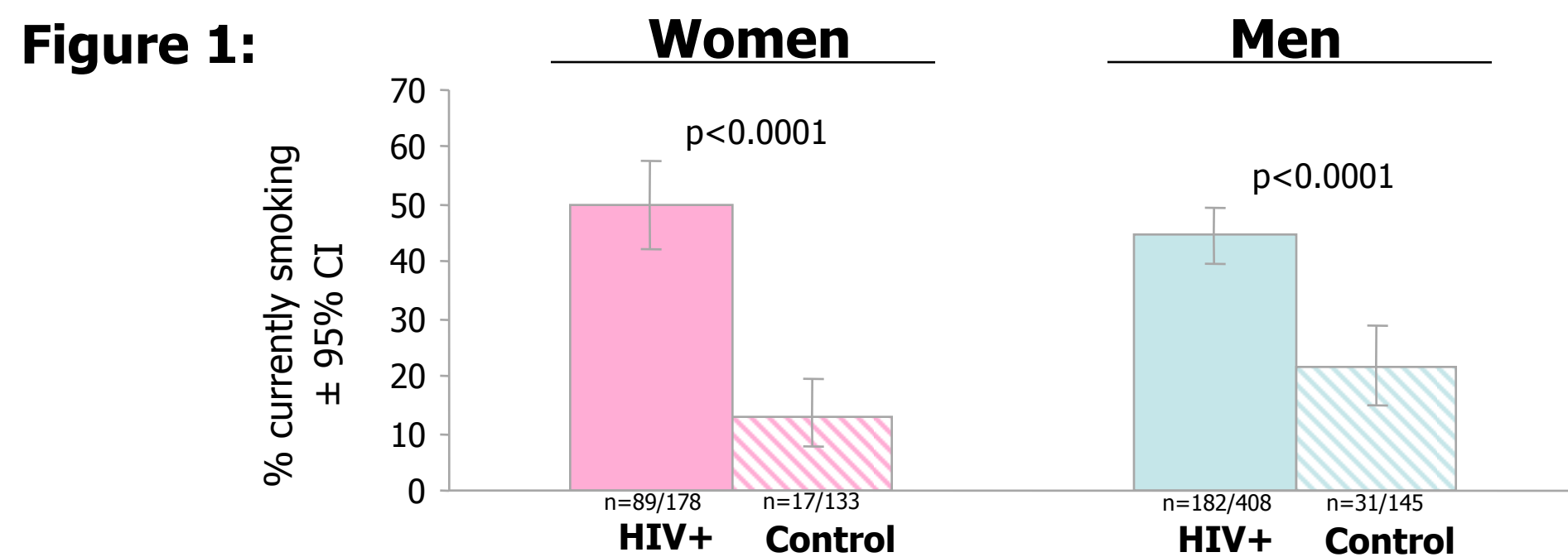
Results

Table 1: Demographic & Clinical Characteristics of HIV+ and Control Subjects

Median (IQR)	Men				Women			
	HIV+ (Not AR)	HIV (AR)	Control	P-value*	HIV+ (Not AR)	HIV (AR)	Control	P-value*
n	774	408	147		329	178	133	
Age (y)	43.0 (38.0-49.0)	40.0 (37.0-43.0)	40.0 (37.0-43.0)	0.93	41.0 (36.0-47.0)	39.0 (36.0-42.0)	42.0 (37.0-44.0)	0.0002
Race: Caucasian	424 (55%)	232 (57%)	81 (55%)	0.043**	111 (34%)	58 (33%)	66 (50%)	0.043**
African American	257 (33%)	124 (30%)	66 (45%)		178 (54%)	98 (55%)	67 (50%)	
Other	93 (12%)	52 (13%)	0		40 (12%)	22 (12%)	0	
FRS ≥ 10%	241 (31%)	65 (16%)	6 (4%)	<.0001	28 (9%)	6 (3%)	1 (1%)	0.25
FRS	6.4% (3.2-12.1)	4.7% (2.8-8.1)	3.7% (2.0-6.4)	0.0002	1.6% (5.0-4.4)	1.1% (0.05-2.6)	1.2% (0.6-2.5)	0.91
DM status***	54 (7%)	21 (5%)	3 (2%)	0.15	33 (10%)	15 (9%)	6 (5%)	0.18
Diastolic BP	80 (72-85)	80 (72-85)	80 (73-86)	0.42	74 (67-81)	72 (66-81)	78 (69-83)	0.006
Systolic BP	117 (108-125)	115 (107-123)	117 (112-127)	0.002	111 (102-122)	108 (99-119)	113 (106-124)	0.001
Current Smoker	321 (41%)	182 (45%)	31 (21%)	<.0001	147 (45%)	89 (50%)	17 (13%)	<.0001
CHD or CVD****	47 (6%)	17 (4%)	0	0.009	16 (5%)	7 (4%)	0	0.022
Total Cholesterol	190 (158-228)	191 (154-227)	202 (178-234)	0.002	191 (160-229)	190 (159-228)	192 (177-215)	0.23
HDL cholesterol	39 (32-48)	38 (31-46)	46 (39-57)	<.0001	49 (38-60)	48 (39-58)	53 (45-62)	0.001
LDL cholesterol	105 (75-132)	104 (75-129)	124 (104-156)	<.0001	105 (79-134)	103 (78-134)	117 (97-139)	0.004
Non-HDL Cholesterol	149 (117-185)	148 (115-181)	151 (129-185)	0.17	139 (111-171)	138 (107-171)	138 (119-165)	0.64
Triglycerides	171 (103-296)	170 (108-294.0)	108 (63-160)	<.0001	135 (89-204)	132 (89-205)	81 (64-118)	<.0001
Lipid Lowering Rx [§]	119 (15%)	45 (11%)	2 (1%)	<.0001	28 (9%)	10 (6%)	2 (2%)	0.08
BMI (kg/m ²)	24 (22-27)	24 (22-27)	27 (25-30)	<.0001	26 (23-32)	26 (22-32)	28 (23-33)	0.13
Waist Circumference	89.0 (82.6-96.3)	88.4 (82.4-95.4)	91.5 (86.8-99.3)	0.0001	87.2 (78.4-97.5)	88.3 (77.3-97.3)	85.6 (74.3-96.2)	0.080
Hip Circumference	93.5 (89.3-98.0)	93.8 (89.4-98.1)	102 (98.0-109)	<.0001	99.2 (91.4-109)	98.9 (91.2-110.2)	105 (98.5-117)	<.0001
WHR	0.95 (0.90-1.00)	0.94 (0.90-0.99)	0.90 (0.86-0.94)	<.0001	0.86 (0.81-0.94)	0.86 (0.81-0.93)	0.77 (0.74-0.84)	<.0001
Leg (L)	2.8 (2.0-4.1)	2.9 (2.0-4.3)	4.6 (3.8-5.8)	<.0001	7.6 (5.1-11.0)	7.3 (5.1-10.8)	10.5 (7.6-14.0)	<.0001
Arm (L)	1.0 (0.8-1.3)	1.0 (0.8-1.3)	1.1 (0.9-1.4)	0.017	1.8 (1.3-2.6)	1.8 (1.2-2.5)	2.3 (1.5-3.0)	0.004
Upper Trunk (L)	2.5 (1.7-3.6)	2.5 (1.7-3.5)	3.1 (2.4-4.2)	<.0001	5.8 (3.5-8.8)	5.9 (3.3-8.8)	5.2 (2.9-8.1)	0.21
Lower Trunk (L)	3.3 (2.1-5.1)	3.3 (2.0-5.3)	5.9 (4.2-7.6)	<.0001	9.5 (5.7-13.4)	9.7 (5.7-13.3)	10.9 (7.1-15.5)	0.020
VAT (L)	1.7 (0.8-3.0)	1.4 (0.7-2.6)	2.0 (1.2-3.0)	0.001	1.5 (0.6-2.4)	1.3 (0.6-2.3)	1.1 (0.5-2.0)	0.055
Total SAT (L)	9.9 (7.0-14.3)	10.1 (7.0-14.9)	14.7 (11.5-19.0)	<.0001	25.6 (16.6-36.8)	25.3 (16.0-36.8)	30.4 (20.0-41.9)	0.021

Note: AR = Age-Restricted to match controls (33-45y); Adipose tissue measures are height-normalized and back-transformed.
 * P-value is HIV (AR) vs. Controls.
 ** Race comparison is proportion of Caucasian vs. African-Americans
 *** Diabetes defined as fasting glucose ≥126 or self-reported insulin or hypoglycemic medication.
 ****CHD or CVD defined as reporting any of the following: heart attack (self-report (SR)), angina (SR), stroke (SR) and self-report indicative of CHD
 § Lipid Lowering Therapy is self-report.

Current Smoking But Not HTN More Prevalent Among HIV+ Subjects



Note: Hypertension defined as systolic BP>140, diastolic>90, or physician diagnosis of hypertension and currently taking antihypertensives (self-report).

Age-restricted and restricted to those with FRS.

Figure 3: Increased VAT and Upper Trunk ARE associated with higher Triglycerides in both HIV+ & Control

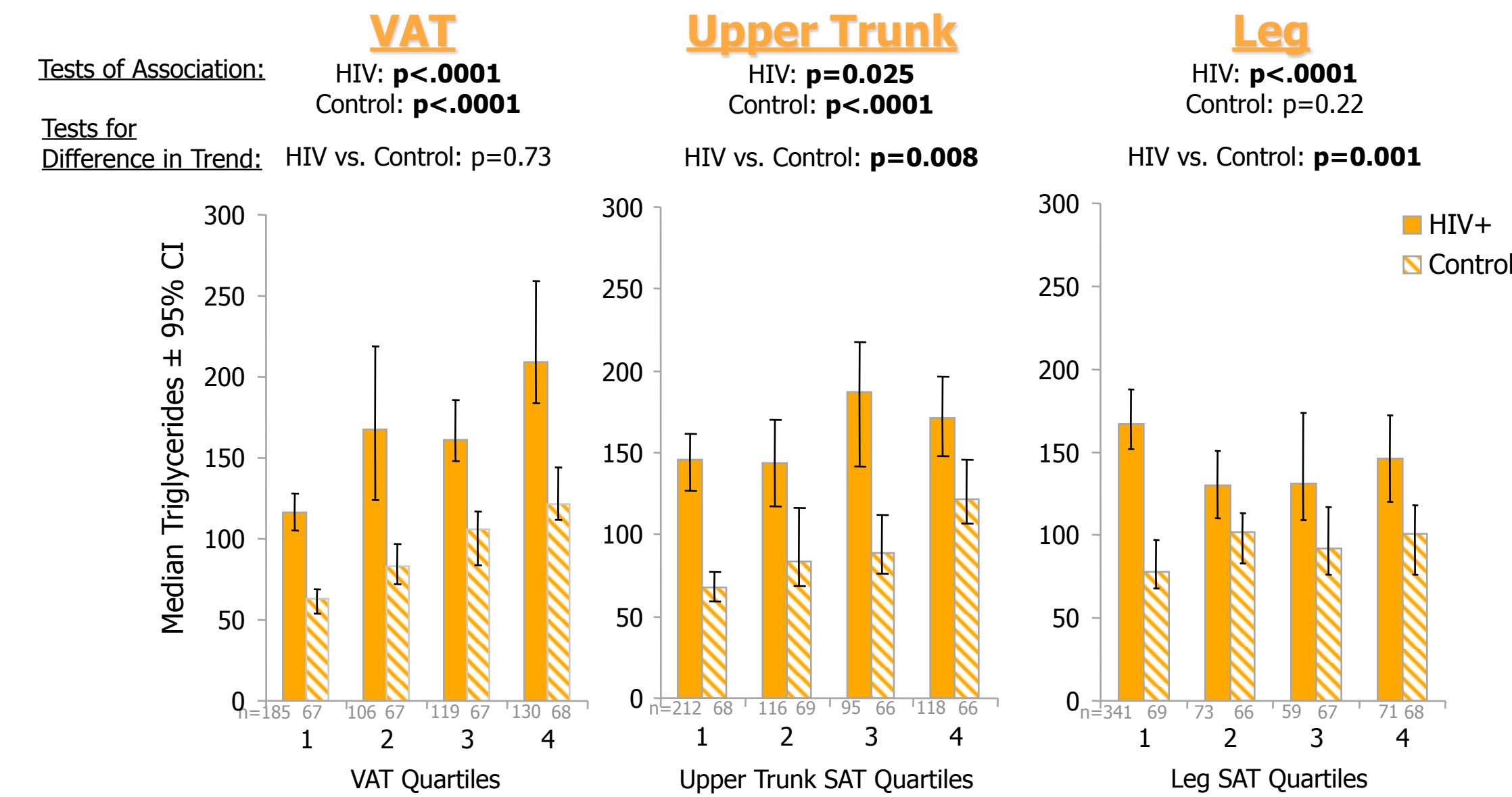


Figure 4: Increased VAT, Upper Trunk & Leg SAT ARE associated with higher LDL in Controls, with a weaker trend in HIV

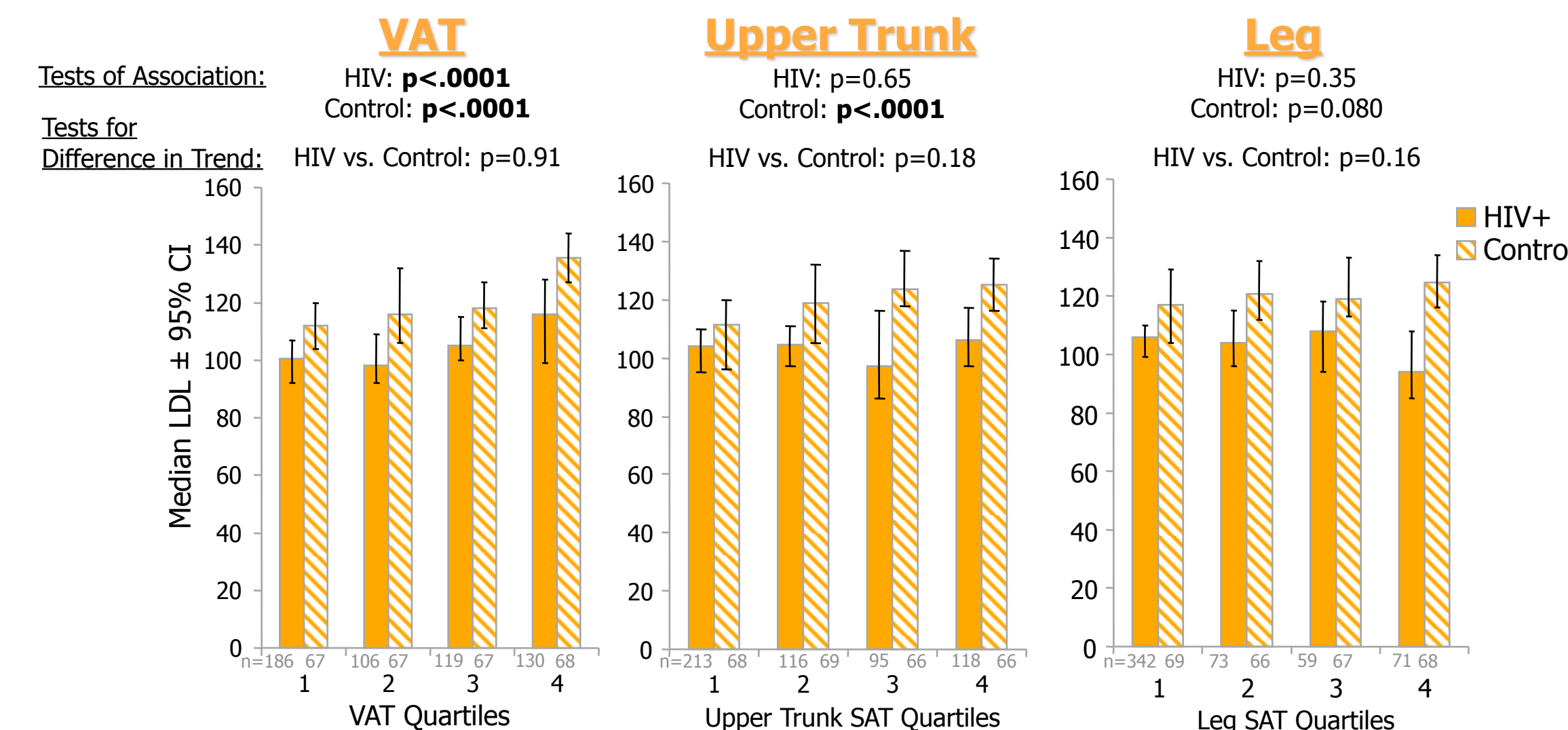
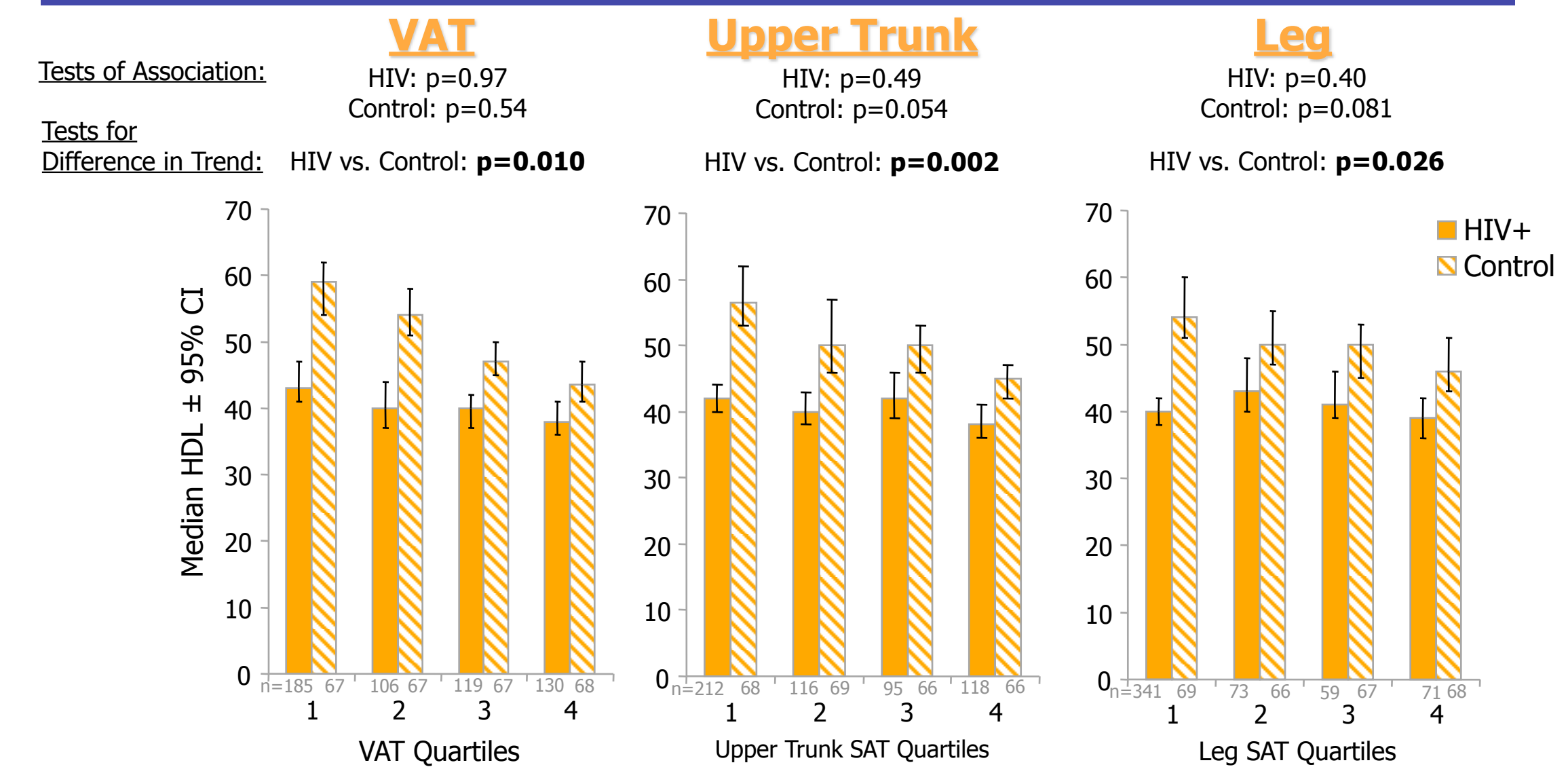


Figure 5: Increased VAT, Upper Trunk & Leg SAT are associated with lower HDL levels in Controls, with a weaker trend in HIV



Note: figures 3-7 represent pooled genders

Figure 6: In HIV+, increased Total Fat, VAT and Upper Trunk ARE associated with higher diabetes prevalence

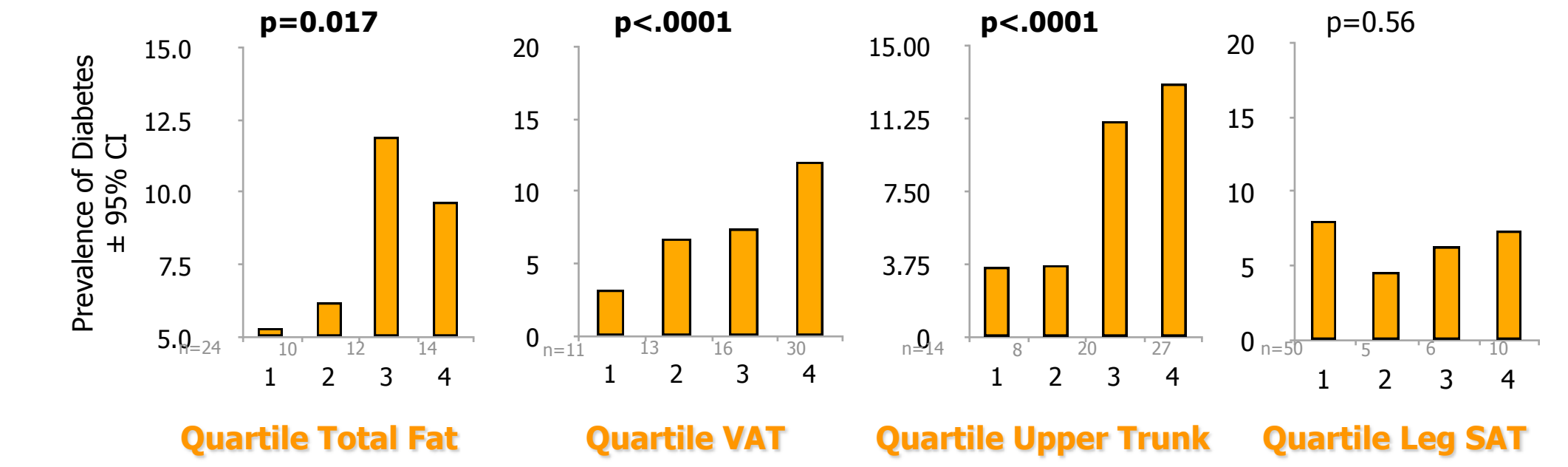
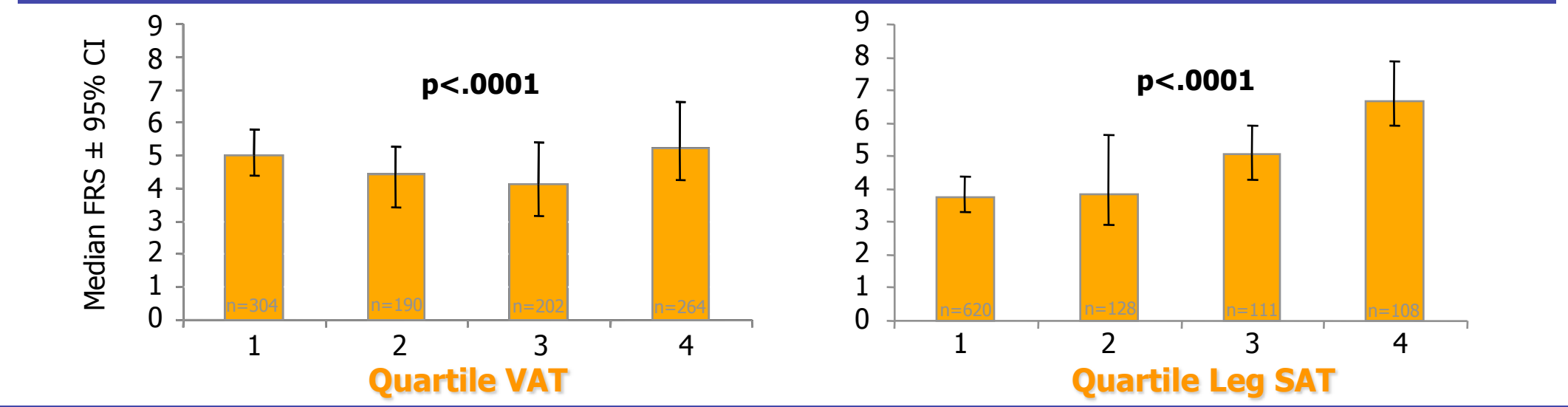


Figure 7: In HIV+, increased VAT & Leg SAT ARE associated with 10-year CVD Framingham Risk Score



Conclusions

- The 10-year CVD Framingham Risk Scores were higher among HIV+ men than Control men. HIV+ and Control women had similarly low CVD risk scores.
- For HIV+ group, increased VAT and decreased SAT were associated with increased CVD risk score.
- For HIV+ men and women and Controls:
 - Increased VAT was associated with higher triglycerides, LDL-c and lower HDL-c.
 - Decreased leg SAT was associated with elevated triglycerides and non-HDL-c levels in HIV+ men and women and Controls.
- In HIV+, increased VAT, total and trunk fat associated with diabetes.
- The associations between regional fat and CVD factors, as well as overall CVD risk should prompt heightened CVD screening and prevention efforts for HIV+ patients with evidence of these fat distributions.

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