Measurement of Abdominal Fat Changes and Predictors of Excess Fat Gain in HIV-Infected Individuals Initiating Therapy

CHIPTS Methods Seminar

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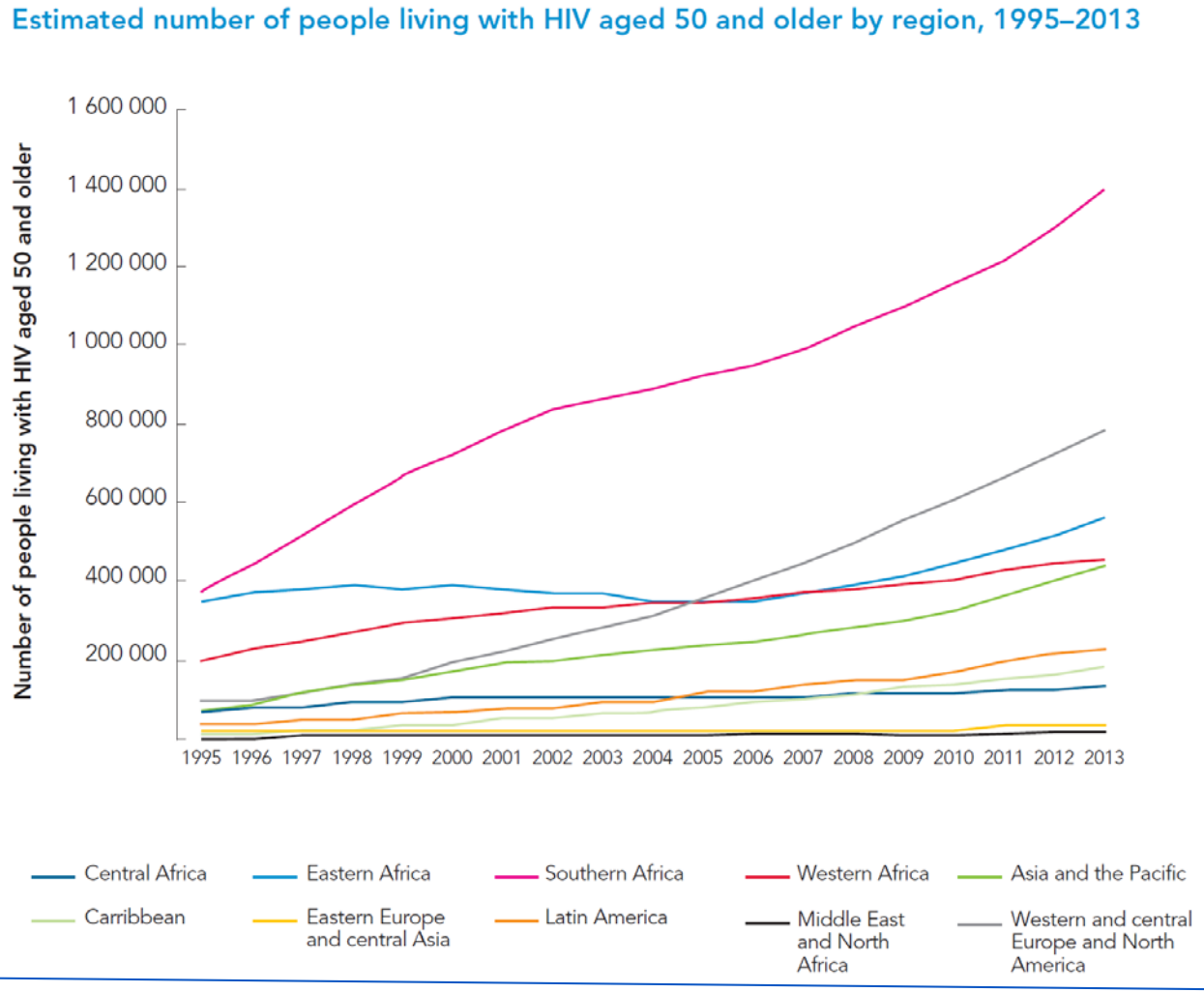
Background

HIV-infected population is aging



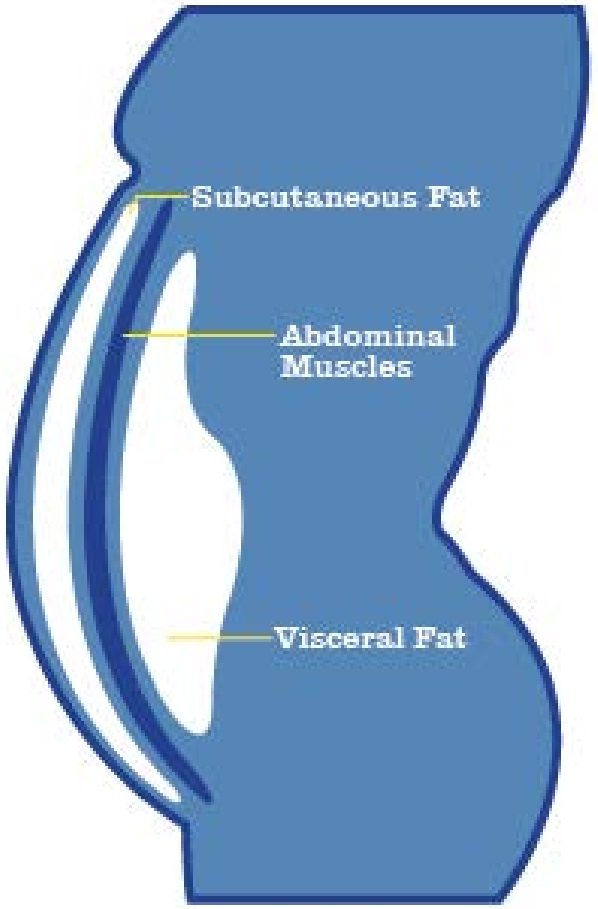
Source: http://www.unaids.org/sites/default/files/media_asset/12_Peopleaged50yearsandolder.pdf

HIV-infected individuals are at a higher risk for cardiovascular disease

- Cardiovascular disease (CVD) is an important cause of morbidity and mortality in HIV-infected individuals
- 1.3-1.7 times greater rate of myocardial infarction compared to uninfected individuals
- Both HIV infection and antiretroviral (ARV) therapy may impact CVD risk

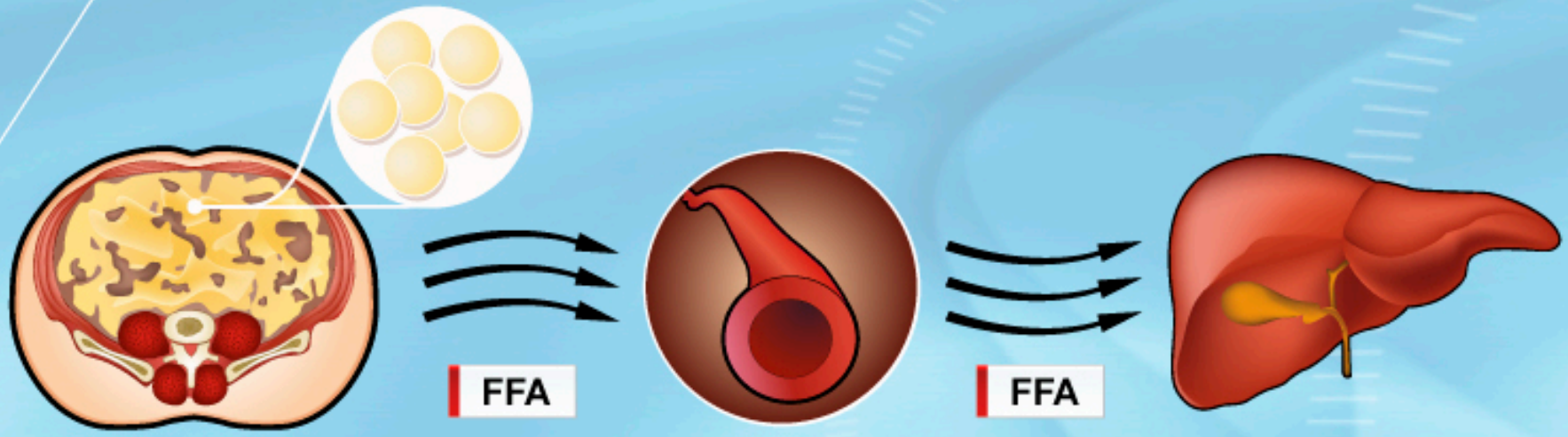
Fat depots and portal vein hypothesis

- ARV therapy has been associated with metabolic complications and fat abnormalities
  - Fat loss and fat gain
- Central fat gain often includes increases in abdominal visceral adipose tissue (VAT)
- VAT has been found to be an important risk factor for cardiovascular disease



http://www.obesityaction.org/educational-resources/resource-articles-2/general-articles/dear-doctor-why-doesnt-liposuction-cure-obesity

SIMPLIFIED MODEL OF THE "PORTAL" THEORY



Release of free fatty acids (FFA) from an expanded, and highly active intra-abdominal adipose tissue depot

Products released from the intra-abdominal depot are drained via the portal vein, leading directly to the liver

Increased exposure to FFA leads to hepatic insulin resistance, fat deposition, lipotoxicity and metabolic derangements

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Overall Objective

- To identify simple approaches to measure and predict excess fat gain in HIV-infected individuals starting antiretroviral therapy
- Study 1: To examine accessible measures of abdominal fat gain
- Study 2: To investigate predictors of abdominal fat gain
- Study 3: To investigate predictors of severe weight gain

Study Populations

ACTG A5257

- Phase III randomized clinical trial from May 2009 to June 2013
- Subjects were randomized in a 1:1:1 ratio to each regimen
  - Raltegravir (RAL) – Integrase inhibitor
  - Darunavir/Ritonavir (DRV/r) – Protease inhibitor
  - Atazanavir/Ritonavir (ATV/r) – Protease inhibitor
  - Each in combination with Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC)
- 1,814 subjects enrolled
  - Treatment-naïve HIV-infected men and women aged 18 or older
- Duration of the study was 96 weeks

ACTG A5260s

- Metabolic substudy of ACTG A5257
  - Evaluates the effects of HIV disease and ARV therapy on cardiovascular and metabolic outcomes
- 334 subjects enrolled
- The duration of the A5260s metabolic substudy was 144 weeks
- Significant increases in trunk fat and visceral fat for all three treatment regimens, but no difference between the study arms

Study 1

Association of Changes in Abdominal Fat with Waist Circumference and Self-Reported Changes in HIV-Infected Individuals

Study 1: Background

- X-ray computed tomography (CT)
  - Measures VAT and total adipose tissue (TAT)
- Dual-energy X-ray absorptiometry (DXA)
  - Measures trunk fat
- Waist circumference
  - Strongly associated with visceral and total abdominal fat

Study 1: Background

- Self-reported measures
  - Self-reported measures may be a valid surrogate for less cost-effective and more labor intensive measures, e.g. DXA and CT
- Limited data concerning the validity of self-reported fat changes

Study 1: Objectives

- **Aim 1:** To determine in ACTG A5260s data whether self-reported changes in abdominal size at week 96 correlate with changes in CT and DXA measurements between study entry and week 96

- **Aim 2:** To determine in ACTG A5260s data if changes in waist circumference correlate with changes in CT and DXA measurements between study entry and week 96 of observation

Study 1: Abdominal Fat Measures

- Substudy subjects from A5260s with DXA and CT measurements from week 0 and week 96 were used for the analysis
- Waist circumference (cm) change between week 0 and week 96
- Self-reported belly size change from week 96 were obtained from the main study data
  - "Lost/No Change"
  - "Gained Some/Somewhat Larger"
  - "Gained A Lot/Much Larger"
- Standard measures
  - DXA: Trunk fat mass (g)
  - CT: Visceral and total abdominal fat (TAT) (cm^2)

Study 1: Stratification variables

- Stratified analyses examining association of waist circumference and self-report with standard measures

- Sex
  - Female, Male
- BMI (kg/m^2)
  - Underweight/Normal (BMI < 24.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2), obese (BMI ≥ 30 kg/m^2)
- Race/Ethnicity
  - White non-Hispanic, black non-Hispanic, Hispanic, Other
- Age
  - 18-30, 31-50, 51-76

Study 1, Aim 1: Methods

- ANOVA to examine differences between group means of both DXA and CT measured fat change across the different self-reported categories
- Linear regression for analyzing any trends between the measured and self-reported data
- Examine gender, race, baseline BMI and age differences

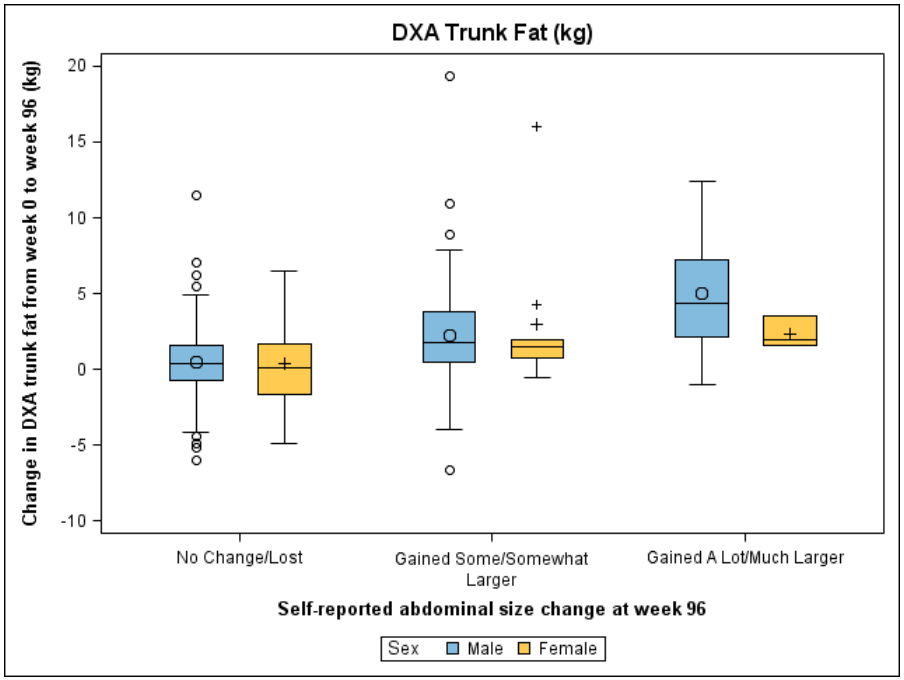
Study 1, Aim 1: Results

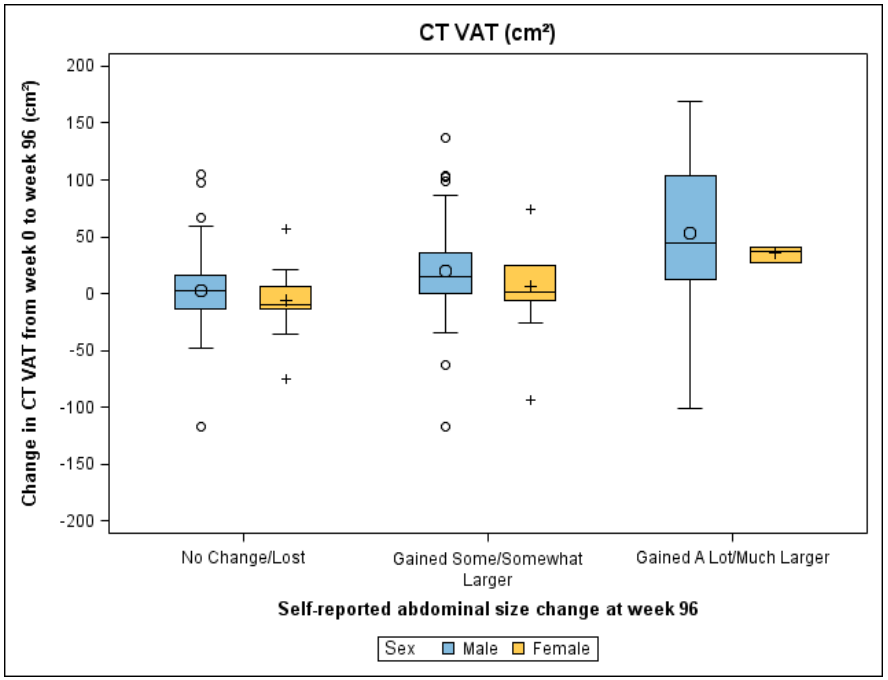
Overall and sex-specific means of trunk fat, VAT, and TAT across self-report abdominal size change categories

	No Change/ Lost		Gained Some/ Somewhat Larger		Gained A Lot/ Much Larger	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Overall						
Trunk fat (kg)	152	0.5 (2.5)	110	2.3 (3.4)	20	4.6 (3.5)
VAT (cm^2)	148	1.7 (28.5)	112	18.7 (37.0)	21	50.1 (58.8)
TAT (cm^2)	148	3.1 (85.2)	112	62.4 (88.1)	21	120.5 (129.2)
Males						
Trunk fat (kg)	134	0.5 (2.4)	101	2.3 (3.2)	17	5.0 (3.7)
VAT (cm^2)	131	2.7 (28.5)	103	19.8 (35.6)	18	52.5 (63.4)
TAT (cm^2)	131	8.4 (69.7)	103	64.0 (88.3)	18	140.6 (114.7)
Females						
Trunk fat (kg)	18	0.4 (3.2)	9	3.0 (5.0)	3	2.3 (1.0)
VAT (cm^2)	17	-5.8 (27.6)	9	6.7 (51.3)	3	35.3 (6.9)
TAT (cm^2)	17	-37.5 (159.0)	9	43.7 (89.1)	3	-0.5 (171.7)

Study 1, Aim 1: Results

Sex-specific change in trunk fat, VAT, and TAT between week 0 and week 96 across self-reported



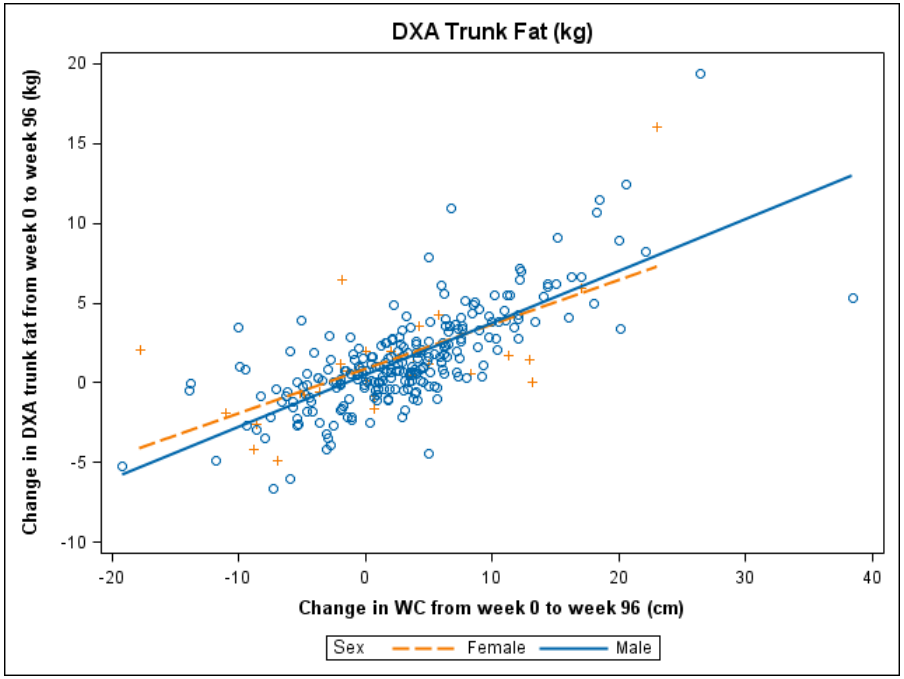


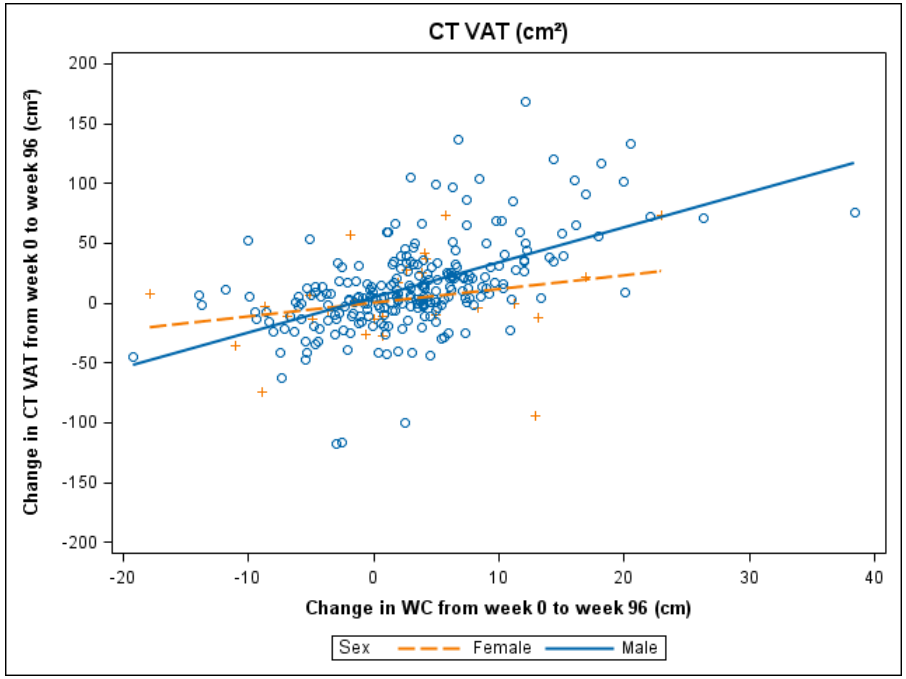
Study 1, Aim 2: Methods

- Pearson correlation to examine correlation between change in waist circumference and change in DXA/CT measurements
- Examined correlation differences between gender, race, baseline BMI and age groups
- Self-reported abdominal changes and waist circumference were compared in a regression model

Study 1, Aim 2: Results

Sex-specific change in trunk fat, VAT, and TAT between week 0 and week 96 across waist circumferences changes





Study 1, Aim 2: Results

Overall and subgroup-specific Pearson correlations between waist circumference and trunk fat, VAT, and TAT changes between week 0 and week 96

	Trunk Fat (kg)			VAT (cm^2)			TAT (cm^2)		
Subgroup	**N**	**ρ**	**p-value**	**N**	**ρ**	**p-value**	**N**	**ρ**	**p-value**
Overall	276	0.72	<.0001	274	0.52	<.0001	274	0.62	<.0001
Sex									
Male	246	0.74	<.0001	246	0.55	<.0001	246	0.71	<.0001
Female	30	0.64	0.0001	28	0.27	0.162	28	0.21	0.282
Baseline BMI (kg/m^2)									
Underweight/Normal: ≤24.9	149	0.69	<.0001	148	0.61	<.0001	148	0.68	<.0001
Overweight: 25-29.9	82	0.83	<.0001	80	0.62	<.0001	80	0.82	<.0001
Obese: ≥30.0	45	0.70	<.0001	46	0.26	0.082	46	0.34	0.021
Race/Ethnicity									
White Non-Hispanic	125	0.73	<.0001	123	0.58	<.0001	123	0.60	<.0001
Black Non-Hispanic	83	0.61	<.0001	83	0.32	0.003	83	0.53	<.0001
Hispanic	55	0.86	<.0001	55	0.64	<.0001	55	0.86	<.0001
Other	12	0.86	0.0004	12	0.45	0.146	12	0.55	0.067
Age (years)									
18-30	79	0.81	<.0001	81	0.46	<.0001	81	0.69	<.0001
31-50	166	0.69	<.0001	163	0.55	<.0001	163	0.59	<.0001
51-76	31	0.67	<.0001	30	0.51	0.004	30	0.60	0.0004

Study 1, Aim 2: Results

Individual predictor and joint models for change in trunk fat, VAT, and TAT between week 0 and week 96

	Trunk Fat (kg)							
	Individual Predictor Models				Joint Model			
	N	R^2	Prob > F	Differential Mean Change (95% CI)	N	R^2	Prob > F	Differential Mean Change (95% CI)
Waist Circumference	276	0.53	<.0001	0.32 (0.28, 0.35)	273	0.54	<.0001	0.30 (0.26, 0.34)
Self-Reported Abdominal Size Change	282	0.15	<.0001		--	--	0.011	
No Change/Lost				ref				ref
Gained Some/ Somewhat Larger				1.85 (1.13. 2.58)				0.42 (-0.16, 1.00)
Gained A Lot/Much Larger				4.13 (2.76, 5.51)				1.62 (0.54, 2.69)

	VAT (cm^2)							
	Individual Predictor Models				Joint Model			
	N	R^2	Prob > F	Differential Mean Change (95% CI)	N	R^2	Prob > F	Differential Mean Change (95% CI)
Waist Circumference	274	0.27	<.0001	2.68 (2.15, 3.22)	272	0.30	<.0001	2.35 (1.78, 2.92)
Self-Reported Abdominal Size Change	281	0.13	<.0001		--	--	0.001	
No Change/Lost				ref				ref
Gained Some/ Somewhat Larger				17.00 (8.37, 25.63)				5.15 (-3.27, 13.56)
Gained A Lot/Much Larger				48.32 (32.26, 64.39)				28.57 (13.21, 43.92)

Study 1: Discussion

- Self-reported abdominal size changes are strongly associated with CT- and DXA-measured abdominal fat changes
- Stratified analyses revealed that the usefulness of self-reported abdominal changes may vary by sex, age, and BMI subgroups
- WC measurements are correlated with abdominal fat changes, specifically CT-measured VAT, both overall and in most subgroups examined
- Between WC and self-reported changes, WC accounts for most of the variability in predicting abdominal fat changes.
- ***Public health implications:*** Waist circumference and self-reported changes could be adopted by clinicians as more affordable methods of monitoring abdominal fat accumulation

Study 2

Role of Treatment and Baseline Predictors on Abdominal Changes in HIV-Infected Individuals Initiating Therapy

Study 2: Objectives

- **Aim 1:** To examine the association of antiretroviral treatments and patient characteristics with waist circumference changes during the study in A5257

- **Aim 2:** To examine the associations of antiretroviral treatments and patient characteristics with self-reported fat changes in A5257

Study 2: Predictors

- *Treatment*
  - ATV/r, DRV/r, and RAL
- *Demographic characteristics*
  - Race/ethnicity, sex, and age (years)
- *Baseline characteristics*
  - BMI (in kg/m^2)
  - CD4+ ($cells/mm^3$)
    - Flow cytometry was used to phenotype CD4+ T-cells.
    - 100 $cells/mm^3$
  - HIV-1 RNA count (copies/mL)
    - Levels were measured using the Abbott RealTime HIV-1 assay
    - Log transformed

Study 2: Outcomes

- *Waist circumference (cm) at week 0 and week 96*

- *Self-reported abdominal size change at week 96*
  - "Lost/No Change"
  - "Gained Some/Somewhat Larger"
  - "Gained A Lot/Much Larger"

Study 2, Aim 1: Methods

- Data for the entire A5257 main study cohort were used for this analysis

- Repeated measures models were implemented to determine the association between predictors and waist circumference gain
  - Examine effect measure modification of treatment by sex and race
  - Examine association of treatment, age, race, sex, and baseline BMI and baseline CD4+/HIV-1 RNA
  - Adjusted for potential confounding from smoking, drinking, illicit drug use, income status, and insurance status

Study 2, Aim 1: Results, ITT Analysis

Treatment arm differences in waist circumference mean changes for overall treatment model and model examining effect measure modification of treatment by sex and race/ethnicity

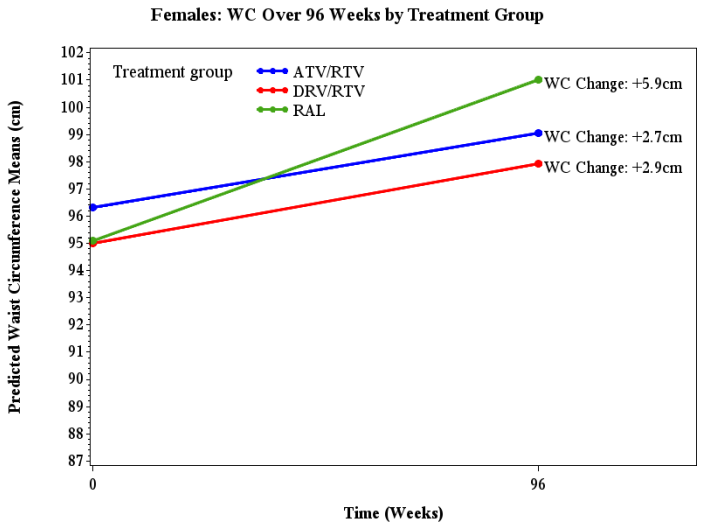
	Model 1: Overall		Model 2: Effect Measure Modification							
			Females versus Males: Differential Mean Change (cm)				Black Non-Hispanic versus Other Race/Ethnicity: Differential Mean Change (cm)			
Treatment Comparison	Differential Mean Change (cm) (95% CI)	p-value	Females	Males	Difference (95% CI)	p-value	Black Non-Hispanic	Other	Difference (95% CI)	p-value
DRV/r - RAL	-1.24 (-2.22, -0.26)	0.0130	-1.53	0.47	-2.01 (-4.32, 0.31)	0.0901	-2.45	0.47	-2.92(-4.92, -0.91)	0.0043
ATV/r - RAL	-0.69 (-1.67, 0.29)	0.1656	-2.95	0.34	-3.28 (-5.65, 0.92)	0.0065	-0.10	0.34	-0.44 (-2.48, 1.60)	0.6720
DRV/r - ATV/r	-0.55 (-1.53, 0.44)	0.2755	1.41	0.14	1.28 (-1.11, 3.66)	0.2933	-2.34	0.14	-2.48 (-4.52, -0.43)	0.0176

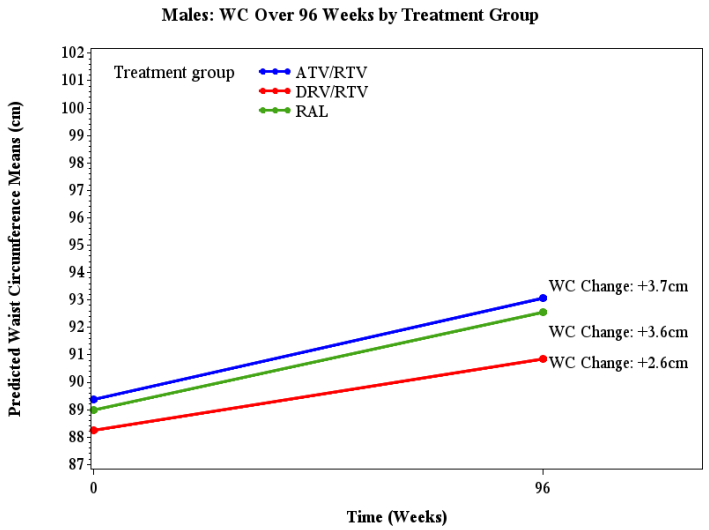
Study 2, Aim 1: Results , ITT Analysis

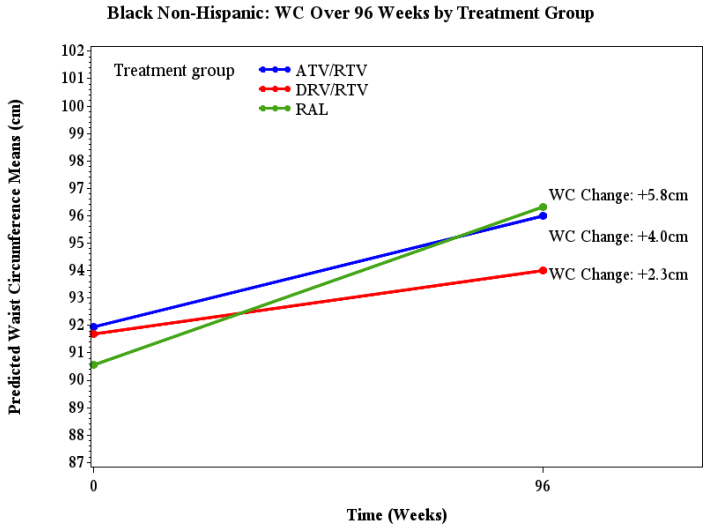
Modification by:

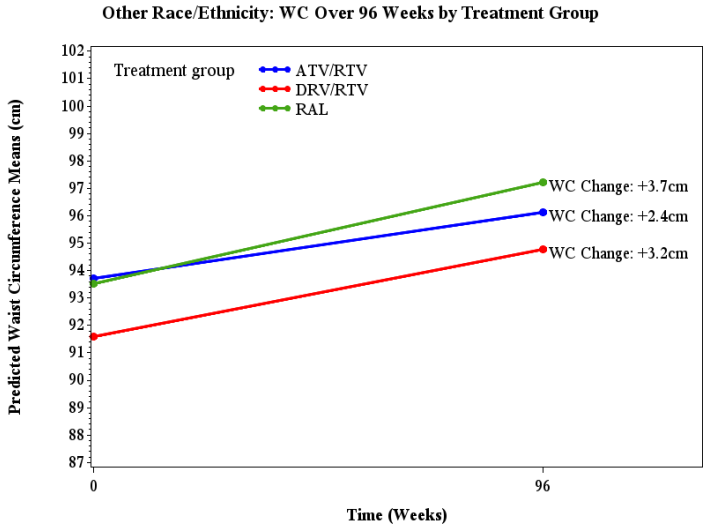
Sex

Race/Ethnicity









Study 2, Aim 1: Results, ITT Analysis

Intention-to-treat analysis of waist circumference mean changes from baseline

	Complete Case Analysis		Imputed Data	
Covariate	**Differential Mean Change (95% CI)**	**p-value**	**Differential Mean Change (95% CI)**	**p-value**
Treatment				
RAL	--	--	--	--
ATV/r	-0.34 (-1.39, 0.71)	0.5210	-0.75 (-1.69, 0.20)	0.1208
DRV/r	-0.70 (-1.75, 0.36)	0.1951	-1.23 (-2.18, -0.28)	0.0108
Sex				
Males	--	--	--	--
Females	0.62 (-0.51, 1.74)	0.2833	0.87 (-0.14, 1.89)	0.0927
Race/Ethnicity				
White Non-Hispanic	--	--	--	--
Black Non-Hispanic	1.05 -0.03, 2.12)	0.0565	0.70 (-0.29, 1.70)	0.1655
Hispanic	-0.10 (-1.40, 1.20)	0.8772	-0.22 (-1.39, 0.94)	0.7060
Other	-1.18 (-3.83, 1.46)	0.3804	-1.96 (-4.46, 0.54)	0.1237
Age (years)	0.0084 (-0.032, 0.049)	0.6854	0.019 (-0.018, 0.055)	0.3198
Baseline BMI (kg/m^2)	0.026 (-0.053, 0.10)	0.5195	0.016 (-0.055, 0.087)	0.6548
Baseline HIV-1 RNA (log_{10} copies/mL)	1.83 (1.13, 2.54)	<.0001	1.85 (1.22, 2.49)	<.0001
Baseline CD4+ (100 cells/mm^3)	-0.65 (-0.91, -0.39)	<.0001	-0.75 (-0.98, -0.51)	<.0001

Study 2, Aim 2: Methods

- Chi-square test to examine if self-reported belly fat is independent of treatment group overall and by sex and race subgroup
- Ordinal logistic regression models examining treatment effects and effect measure modification of treatment
- Ordinal logistic regression model examining association between specific ARVs, age, sex, race/ethnicity, baseline BMI, baseline CD4+/HIV-1 RNA and odds of self-reported fat gain, adjusting for confounding
  - Crude models examining individual covariates
  - Complete case analysis
  - Multiple imputation analysis

Study 2, Aim 2: Results, ITT analysis

Odds of reporting a higher category of self-reported abdominal size change

	Complete Case Analysis		Imputed Data	
Covariate	**Odds Ratio (95% CI)**	**p-value**	**Odds Ratio (95% CI)**	**p-value**
Treatment				
RAL	--	--	--	--
ATV/r	0.95 (0.72, 1.26)	0.736	1.05 (0.82, 1.34)	0.696
DRV/r	0.92 (0.70, 1.21)	0.547	0.97 (0.76, 1.24)	0.825
Sex				
Males	--	--	--	--
Females	1.34 (1.00, 1.80)	0.050	1.36 (1.05, 1.76)	0.021
Race/Ethnicity				
White Non-Hispanic	--	--	--	--
Black Non-Hispanic	0.99 (0.75, 1.32)	0.957	0.95 (0.74, 1.23)	0.703
Hispanic	0.83 (0.59, 1.17)	0.279	0.74 (0.55, 1.01)	0.055
Other	0.67 (0.32, 1.42)	0.301	0.59 (0.29, 1.19)	0.139
Age (years)	1.01 (0.997, 1.02)	0.175	1.01 (0.999, 1.02)	0.078
Baseline BMI (kg/m^2)	1.03 (1.01, 1.05)	0.004	1.04 (1.02, 1.06)	<.0001
Baseline HIV-1 RNA (log_{10} copies/mL)	1.30 (1.08, 1.57)	0.006	1.35 (1.14, 1.59)	0.0004
Baseline CD4+ (100 cells/mm^3)	0.88 (0.82, 0.95)	0.0005	0.88 (0.83, 0.94)	0.0001

Study 2: Discussion

- Results indicated that the treatment effect on WC gains was modified by sex and race/ethnicity
  - Previous research has shown that metabolic effects of treatment may be modified by patient characteristics

- Baseline disease state was strongly associated with abdominal changes over 96 weeks through both self-report and WC outcomes.
  - May be due to HIV-infected macrophages that exacerbate inflammation in the adipose tissue and lead to their expansion

- ***Public health implications:*** Understanding predictors of abdominal fat gain, a highly prevalent issue, may help physicians optimize treatment approaches to prevent fat accumulation

Study 3

Predictors of Severe Weight Gain or Clinically Meaningful Increases in BMI After Antiretroviral Initiation

Study 3: Background

- Antiretroviral therapy has led to individuals regaining their weight as a "return to health"
- Overweight/obesity is now becoming more common in the HIV-infected population
- Benefits from weight gain may not persist in overweight individuals

Study 3: Objective

- To identify whether certain demographics and baseline clinical characteristics are associated with severe weight gain in HIV-infected individuals

Study 3: Predictors

- *Treatment*
  - ATV/r, DRV/r, and RAL
- *Demographic characteristics*
  - Race/ethnicity, sex, and age (years)
- *Baseline characteristics*
  - BMI (in kg/m^2)
  - CD4+ ($cells/mm^3$)
    - Flow cytometry was used to phenotype CD4+ T-cells.
    - 100 $cells/mm^3$
  - HIV-1 RNA count (copies/mL)
    - Levels were measured using the Abbott RealTime HIV-1 assay
    - Log transformed

Study 3: Outcomes

- Extreme fat gain defined by two methods:
  1. *Severe weight gain*
     - Normal at baseline: ≥ 10% gain in weight
     - Underweight at baseline: Increase more than two BMI categories and had ≥ 10% gain in weight
  2. *Severe BMI gain*
     - Categories include: **Underweight** (BMI < 18.5 kg/m^2), **normal** (BMI 18.5-24.9 kg/m^2), **overweight** (BMI 25-29.9 kg/m^2), **obese** (BMI 30-39.9 kg/m^2), **morbid obese** (BMI 40-49.9 kg/m^2), and **super obese** (BMI ≥ 50 kg/m^2)
     - Normal at baseline: Moved upward at least one BMI category
     - Underweight at baseline: Increase more than two BMI categories

Study 3: Methods

- Logistic regression modeling was used to examine predictors of both severe percent weight increases and increases in clinical BMI status.

- Multivariable models including all predictors of interest were examined for each weight gain outcome.
  - These models were adjusted for potential confounding from smoking, drinking, illicit drug use, income status, and insurance status.

Study 3: Results – severe weight gain

Crude and adjusted logistic regression models predicting ***severe weight gain***

	Crude		Adjusted			
			Complete Case Analysis		Imputed Data Analysis	
Covariate	**Odds Ratio (95% CI)**	**p-value**	**Odds Ratio (95% CI)**	**p-value**	**Odds Ratio (95% CI)**	**p-value**
Treatment						
RAL	--	--	--	--	--	--
ATV/r	0.76 (0.57, 1.01)	0.057	0.77 (0.54, 1.12)	0.175	0.72 (0.53, 0.99)	0.043
DRV/r	0.77 (0.58, 1.02)	0.071	0.81 (0.56, 1.17)	0.251	0.74 (0.54, 1.01)	0.056
Sex						
Males	--	--	--	--	--	--
Females	1.31 (1.01, 1.70)	0.045	1.24 (0.84, 1.83)	0.288	1.35 (0.97, 1.89)	0.074
Race/Ethnicity						
White Non-Hispanic	--	--	--	--	--	--
Black Non-Hispanic	1.69 (1.28, 2.23)	0.0002	1.74 (1.17, 2.58)	0.006	1.55 (1.10, 2.20)	0.013
Hispanic	1.61 (1.17, 2.23)	0.004	1.13 (0.71, 1.79)	0.603	0.99 (0.67, 1.48)	0.976
Other	0.64 (0.24, 1.67)	0.359	0.78 (0.27, 2.32)	0.659	0.50 (0.17, 1.45)	0.202
Age (years)	1.01 (0.998, 1.02)	0.125	1.01 (0.996, 1.03)	0.160	1.01 (0.99, 1.02)	0.286
Baseline BMI (kg/m^2)	0.96 (0.94, 0.98)	0.0004	0.99 (0.96, 1.02)	0.541	0.98 (0.96, 1.01)	0.177
Baseline HIV-1 RNA (log_{10} copies/mL)	3.45 (2.84, 4.19)	<.0001	2.89 (2.20, 3.80)	<.0001	2.52 (2.00, 3.16)	<.0001
Baseline CD4+ (100 cells/mm^3)	0.62 (0.58, 0.67)	<.0001	0.80 (0.73, 0.89)	<.0001	0.78 (0.72, 0.85)	<.0001

Study 3: Results – severe BMI gain

Crude and adjusted logistic regression models predicting ***severe BMI gain***

	Crude		Adjusted			
			Complete Case Analysis		Imputed Data Analysis	
Covariate	**Odds Ratio (95% CI)**	**p-value**	**Odds Ratio (95% CI)**	**p-value**	**Odds Ratio (95% CI)**	**p-value**
Treatment						
RAL	--	--	--	--	--	--
ATV/r	0.85 (0.64, 1.13)	0.2739	0.91 (0.64, 1.30)	0.6156	0.83 (0.62, 1.13)	0.2381
DRV/r	0.77 (0.58, 1.03)	0.0737	0.78 (0.54, 1.12)	0.1745	0.73 (0.53, 0.99)	0.0414
Sex						
Males	--	--	--	--	--	--
Females	1.33 (1.02, 1.74)	0.0347	1.11 (0.76, 1.62)	0.5779	1.14 (0.83, 1.58)	0.4085
Race/Ethnicity						
White Non-Hispanic	--	--	--	--	--	--
Black Non-Hispanic	1.60 (1.20, 2.12)	0.0012	1.56 (1.07, 2.29)	0.0218	1.48 (1.06, 2.08)	0.0217
Hispanic	1.93 (1.40, 2.67)	<.0001	1.44 (0.93, 2.23)	0.1011	1.44 (0.99, 2.10)	0.0555
Other	0.52 (0.18, 1.50)	0.2260	0.68 (0.22, 2.10)	0.5050	0.48 (0.16, 1.43)	0.1851
Age (years)	1.01 (0.999, 1.02)	0.0653	1.01 (0.99, 1.02)	0.3956	1.01 (0.995, 1.02)	0.2407
Baseline BMI (kg/m^2)	1.01 (0.99, 1.03)	0.5888	1.04 (1.01, 1.07)	0.0106	1.03 (1.00, 1.05)	0.0375
Baseline HIV-1 RNA (log_{10} copies/mL)	2.32 (1.94, 2.77)	<.0001	2.11 (1.64, 2.73)	<.0001	1.79 (1.44, 2.22)	<.0001
Baseline CD4+ (100 cells/mm^3)	0.69 (0.64, 0.74)	<.0001	0.83 (0.76, 0.92)	0.0002	0.79 (0.73, 0.86)	<.0001

Study 3: Discussion

- Treatment with a protease inhibitor may be protective against severe weight/BMI gain compared to Raltegravir
- Being black non-Hispanic was significantly associated with an increased odds of severe weight/BMI gain
- We also found a strong association between baseline disease state before ART initiation and increased odds of severe weight/BMI gain
- ***Public health implications:*** As the prevalence of overweight/obesity increases, understanding characteristics associated with weight gain may help manage CVD risk and metabolic complications

Overall Summary

Overall Strengths and Limitations

Strengths

- Collected CT/DXA measurements
- Longitudinal study to examine changes in abdominal fat and weight over 96 weeks
- High-quality clinical trial data
- Large sample size and diverse population for subgroup analyses

Limitations

- Attrition resulting from loss to follow-up
- Missing data on covariates
- Results may not be generalizable to other target populations
- Data on diet and exercise was not collected

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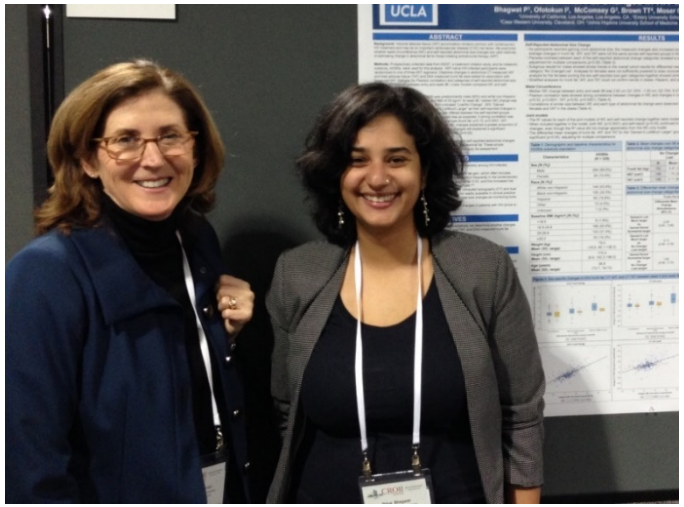

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