



# Long-term Changes in Body Composition among HIV-infected Antiretroviral Naive Persons Randomized to PI vs. NNRTI vs. PI + NNRTI-based Antiretroviral Regimens: Results of the CPCRA 061 Metabolic Study

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## ABSTRACT

**BACKGROUND** Information on long-term changes in body composition (BC) following initiation of different antiretroviral treatment (ART) strategies is limited.

**METHODS** We compared changes in BC in 422 patients randomized to 1 of 3 treatment strategies: PI (N=141), NNRTI (N=141), or PI+NNRTI (N=140) containing regimens (with NRTI(s)). At baseline and 4-month intervals, fat-free mass (FFM) and total body fat (TBF) were measured using bioelectric impedance analysis. Subcutaneous tissue areas (STA) and non-STAs (NSTA) of midarm and midhigh, and STA and visceral tissue area (VTA) of waist were calculated from anthropometric measurements. Rates of change (unit/month) and mean change (unit) were compared by ART strategy.

**RESULTS** Median age was 38 years; 22% were women; 60% African American, and 10% Latino/a. Median follow-up was 5 years. Rates of change (i.e., slopes) after first follow-up visit were:

	FFM (kg/mo)	TBF (kg/mo)	Midarm STA (cm <sup>2</sup> /mo)	Midarm NSTA (cm <sup>2</sup> /mo)
PI	0.03*	0.01	-0.12*	0.11*
NNRTI	0.02*	-0.02	-0.13*	0.05*
PI + NNRTI	0.02*	0.00	-0.14*	0.08*

	Midhigh STA (cm <sup>2</sup> /mo)	Midarm NSTA (cm <sup>2</sup> /mo)	Waist STA (cm <sup>2</sup> /mo)	Waist VTA (cm <sup>2</sup> /mo)
PI	-0.15*	0.06	-0.17	0.73*
NNRTI	-0.23*	-0.20*	-0.39*	0.58*
PI + NNRTI	-0.25*	-0.09	-0.27*	0.72*

(\* p-value < 0.05).

Neither rates of change nor mean change varied by strategy group. For all strategies, significant mean increases were observed in FFM and TBF, and in NSTA of midarm, midhigh, and waist VTA. The waist STA significantly increased in PI and PI+NNRTI strategies only.

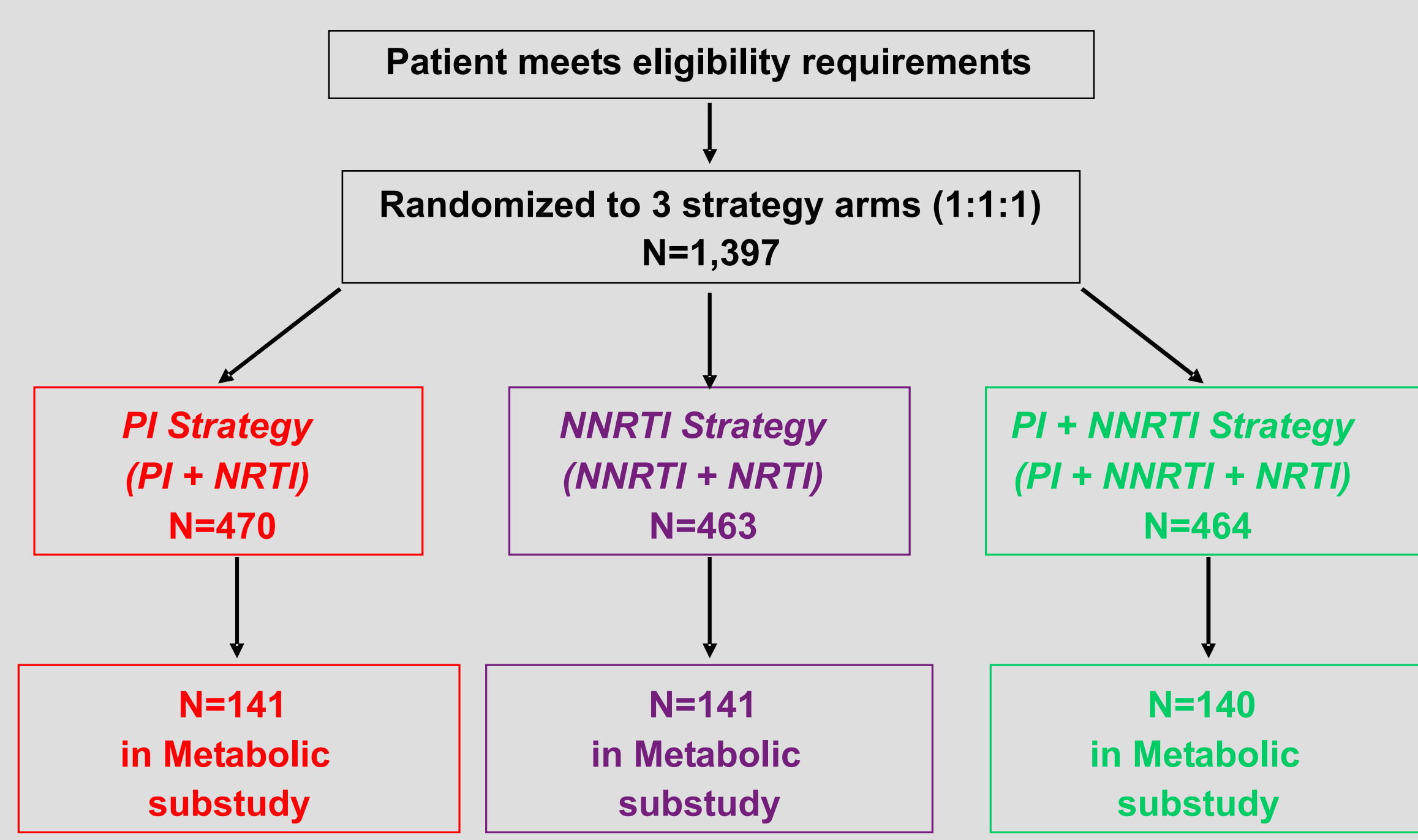
**CONCLUSIONS** In this prospective trial, changes in total and regional body fat did not differ by ART strategy, with losses demonstrated in STAs and gains in FFM, NSTAs, and VTA. In contradistinction to other studies, there was no significant difference by planned ART.

## OBJECTIVE

- To assess changes in body composition in a substudy of ART-naïve patients randomized to three highly active antiretroviral regimens, in the Flexible Initial Retrovirus Suppressive Therapies (FIRST) Study (CPCRA 058), a multi-center, randomized clinical trial to compare initial ART with PI, NNRTI or PI + NNRTI all with NRTI(s)

## METHODS

### STUDY DESIGN



### ELIGIBILITY CRITERIA

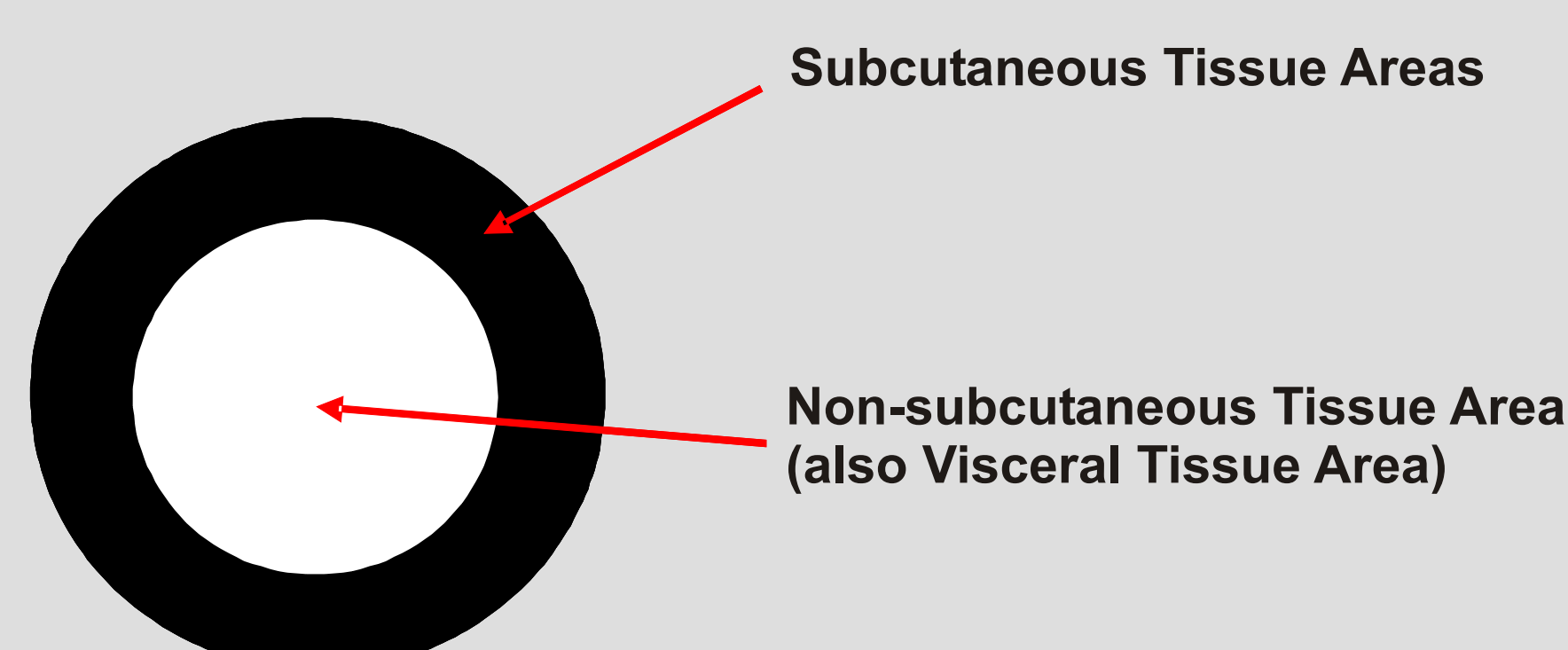
- Inclusion Criteria**
- Documented HIV infection
  - At least 13 years of age
  - Signed informed consent approved by local IRBs

- Exclusion Criteria**
- Women if pregnant or breast feeding
  - Prior use of PI or NNRTI
  - More than 4 weeks of NRTI or > 1 week of 3TC

### MEASURES OF BODY COMPOSITION

- Height and weight
- Body circumferences- midarm, waist, hip, midhigh,
- Skinfolds- triceps, suprascapular, subscapular, abdomen and midhigh
- Total body fat and fat free mass [by bioelectric impedance analysis (BIA)]
- Subcutaneous tissue areas and non-subcutaneous (also visceral) tissue areas

### Cross Section of Midarm, Waist, or Midhigh



### STATISTICAL ANALYSIS

- Intent-to-treat
- Analysis of variance used to compare mean change from baseline adjusted for baseline value
  - For early change
    - mean change from month 4 calculated
  - For overall change
    - mean change from all follow-up measurements calculated
- Repeat measurement analyses with random intercepts and random slopes linear regression lines fitted to follow-up data, beginning at month 4
  - Slopes of lines used to estimate rates of change

## RESULTS

### Baseline Characteristics

	PI (N = 141)	NNRTI (N = 140)	PI + NNRTI (N = 140)
Age (years)	37	38	39
Female (%)	26	23	17
Race			
African American (%)	61	62	59
Prior AIDS (%)	38	39	32
CD4 (cells/mm <sup>3</sup> )	235	206	204
RNA (log <sub>10</sub> copies/mL)	4.9	5.0	5.0

### ART Prescribed after Randomization

	PI (N = 141)	NNRTI (N = 140)	PI + NNRTI (N = 140)
PI (%)			
NFV	58	0	64
IDV	12	0	11
RTV-boosted	26	0	22
Other	4	0	2
NNRTI (%)			
EFV	0	63	50
NVP	1	37	49
Other	0	0	1
NRTI (%)			
ZDV + 3TC	53	53	38
d4T + 3TC	19	19	10
ABC + 3CT	11	12	16
ddI + d4T	12	12	14
Single NRTI	0	0	19
Other	6	4	2

### Mean Change from Baseline by Treatment Strategy

Outcome Measures	Mean Change to Four Months Follow-Up			P**	Mean Change for all Follow-Up Visits			P**
	PI Strategy	NNRTI Strategy	PI + NNRTI Strategy		PI Strategy	NNRTI Strategy	PI + NNRTI Strategy	
Number of Patients	136	135	131		140	141	136	
Body Mass								
Total body fat (kg)	1.46 (<0.005)	1.40 (<0.005)	1.33 (<0.005)	0.98	2.06 (<0.005)	1.64 (<0.005)	1.75 (<0.005)	0.79
Fat free mass (kg)	1.20 (<0.005)	1.43 (<0.005)	1.04 (<0.005)	0.56	1.92 (<0.005)	2.02 (<0.005)	1.79 (<0.005)	0.88
Weight (kg)	2.60 (<0.005)	2.86 (<0.005)	2.32 (<0.005)	0.78	4.19 (<0.005)	3.91 (<0.005)	3.69 (<0.005)	0.87
Body mass index (kg/m <sup>3</sup> )	0.87 (<0.005)	0.96 (<0.005)	0.76 (<0.005)	0.65	1.40 (<0.005)	1.33 (<0.005)	1.22 (<0.005)	0.98
Midarm								
Subcutaneous tissue area (cm <sup>2</sup> )	2.20 (<0.005)	1.88 (<0.005)	1.46 (0.01)	0.81	0.69 (0.28)	-0.01 (0.99)	-0.05 (0.45)	0.81
Non-subcutaneous tissue area (cm <sup>2</sup> )	1.36 (0.02)	2.62 (<0.005)	1.69 (0.03)	0.31	3.17 (<0.005)	4.21 (<0.005)	3.61 (<0.005)	0.34
Waist								
Subcutaneous tissue area (cm <sup>2</sup> )	7.61 (<0.005)	8.41 (<0.005)	13.72 (<0.005)	0.15	6.42 (0.01)	4.10 (0.18)	8.74 (<0.005)	0.44
Visceral tissue area (cm <sup>2</sup> )	20.02 (<0.005)	25.19 (<0.005)	9.95 (<0.005)	0.29	34.85 (<0.005)	35.56 (<0.005)	32.50 (<0.005)	0.98
Midhigh								
Subcutaneous tissue area (cm <sup>2</sup> )	3.10 (<0.005)	4.94 (<0.005)	4.14 (<0.005)	0.53	2.26 (0.06)	2.48 (0.04)	1.32 (0.26)	0.86
Non-subcutaneous tissue area (cm <sup>2</sup> )	5.33 (<0.005)	11.73 (0.01)	1.60 (0.42)	0.07	8.06 (<0.005)	6.57 (<0.005)	5.01 (0.02)	0.96

\* P-value for comparing mean change to zero.

\*\* P-values for comparing the three means adjusted for baseline measurement.

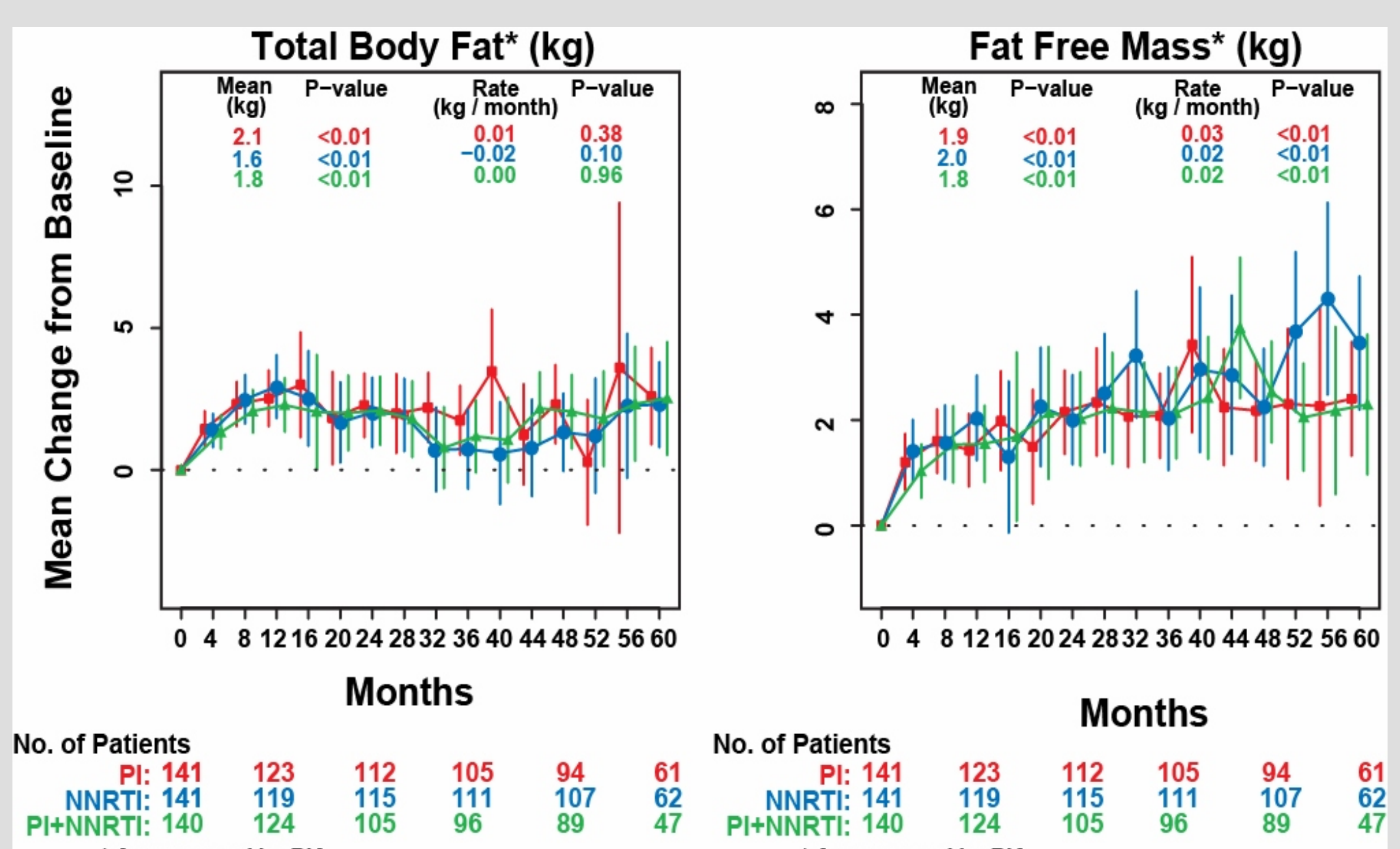
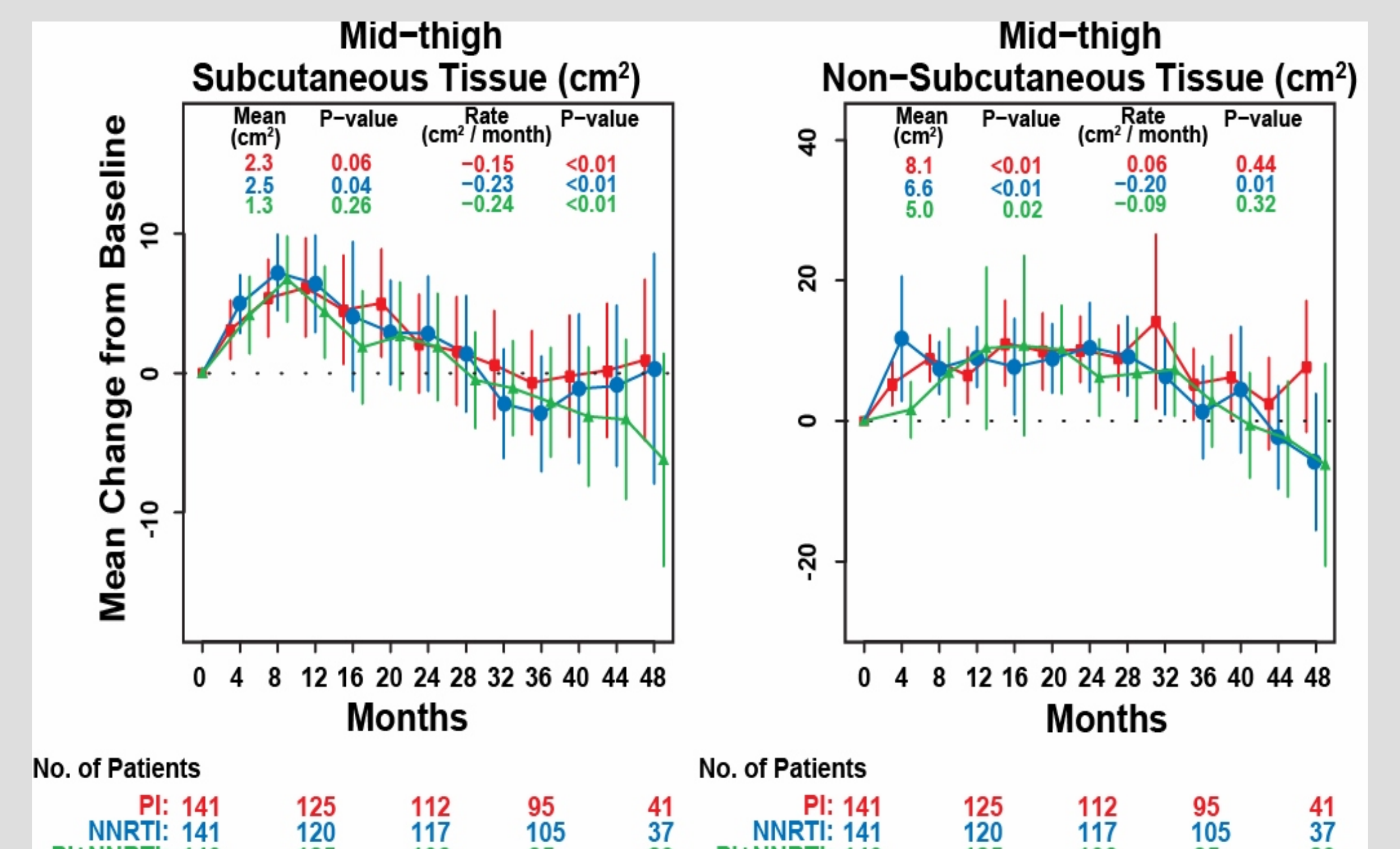
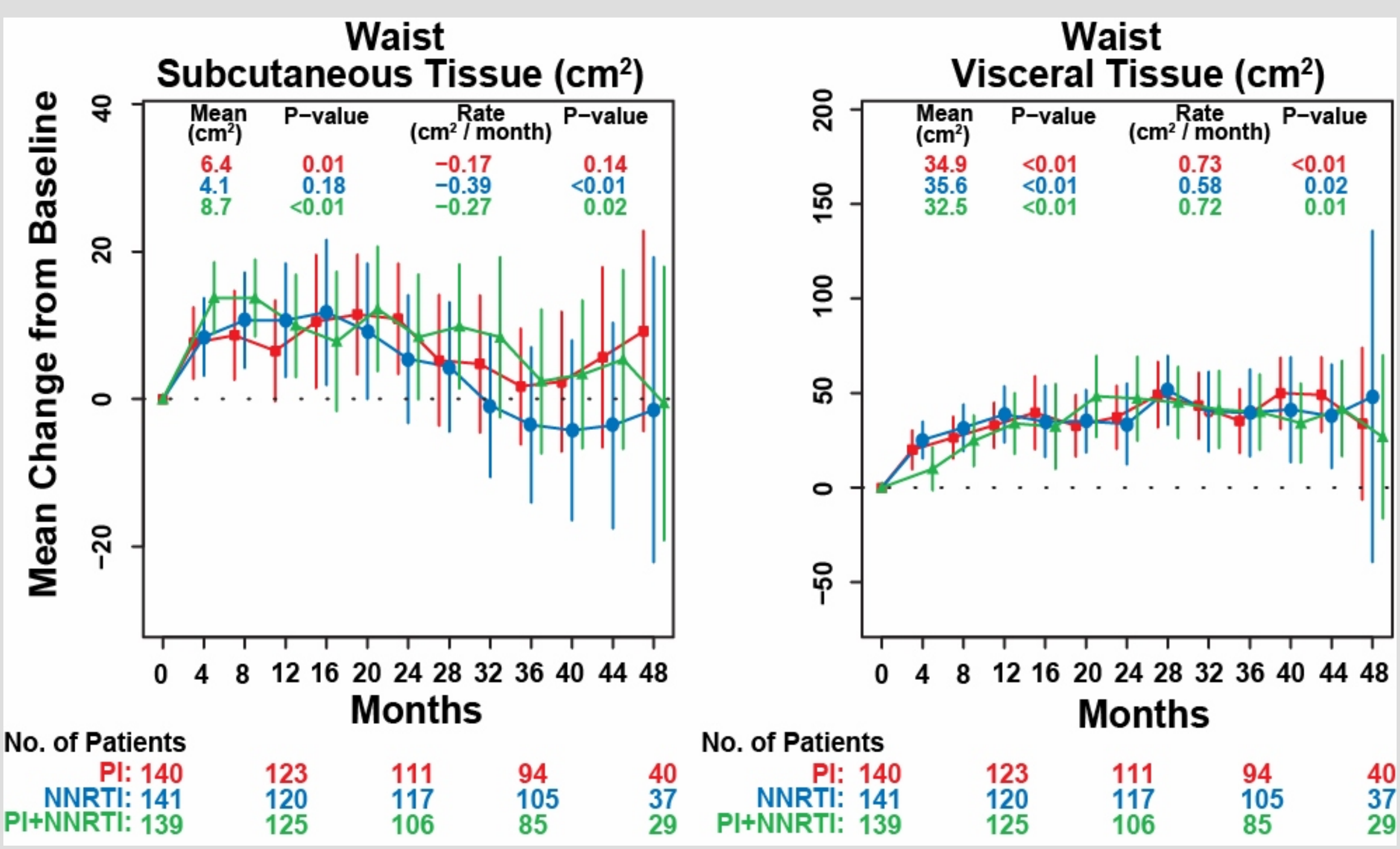
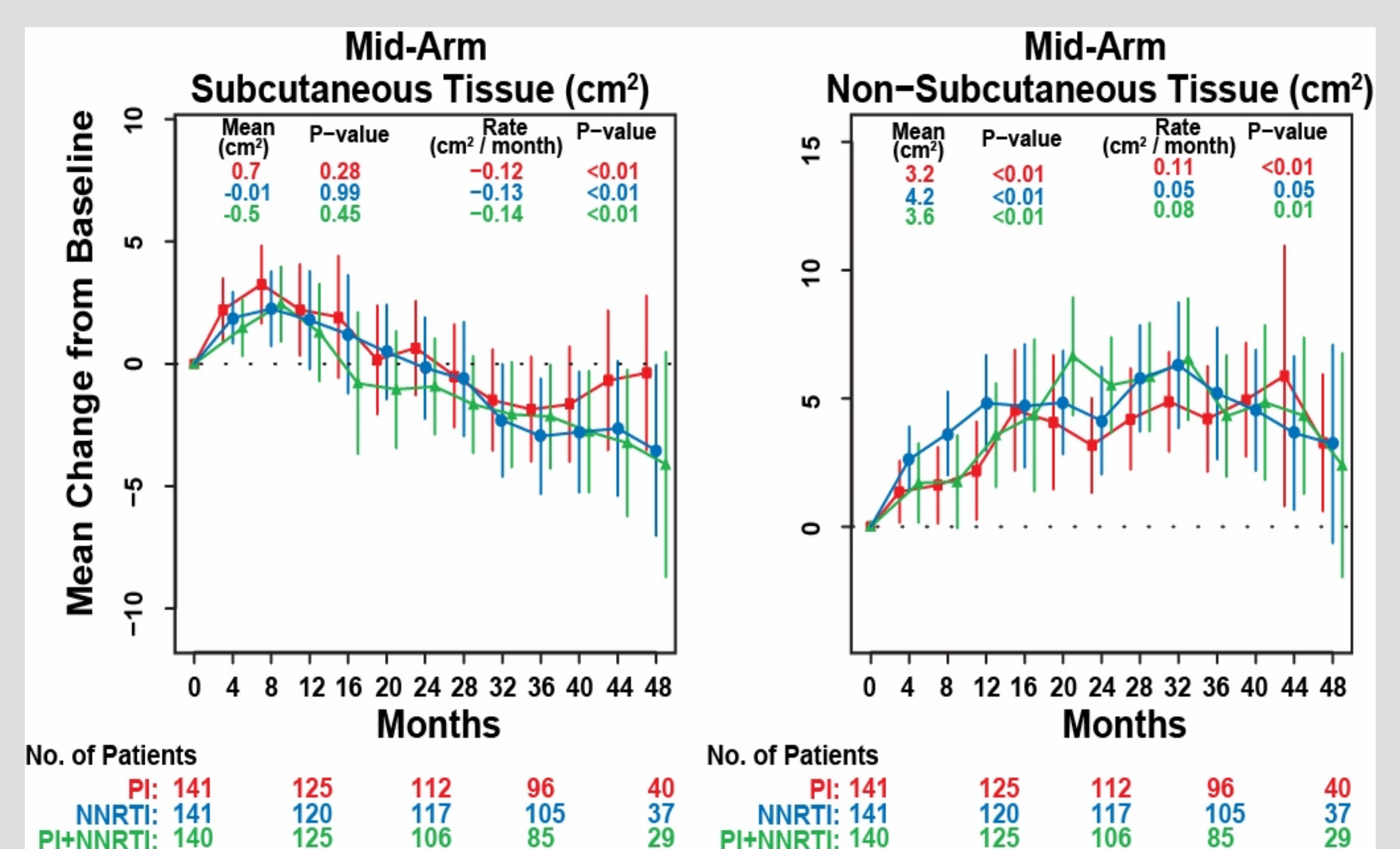
### Regression Coefficients for Each Measure of Body Composition by Treatment Strategy

Outcome Measures	PI Strategy	NNRTI Strategy	PI + NNRTI Strategy	P-value**
	Slope (P*)	Slope (P*)	Slope (P*)	
Number of Patients	140	141	136	
Body Mass				
Total body fat (kg)	0.011 (0.38)	-0.020 (0.10)	0.001 (0.96)	0.19
Fat free mass (kg)	0.027 (<0.005)	0.024 (<0.005)	0.024 (<0.005)	0.94
Weight (kg)	0.039 (0.01)	0.012 (0.43)	0.032 (0.07)	0.48
Body mass index (kg/m <sup>3</sup> )	0.012 (0.03)	0.004 (0.51)	0.011 (0.06)	0.49
Midarm				
Subcutaneous tissue area (cm <sup>2</sup> )	-0.119 (<0.005)	-0.127 (<0.005)	-0.137 (<0.005)	0.90
Non-subcutaneous tissue area (cm <sup>2</sup> )	0.113 (<0.005)	0.053 (0.05)	0.061 (0.01)	0.32
Waist				
Subcutaneous tissue area (cm <sup>2</sup> )	-0.174 (0.14)	-0.389 (<0.005)	-0.273 (0.02)	0.43
Visceral tissue area (cm <sup>2</sup> )	0.733 (<0.005)	0.577 (0.02)	1.0721 (0.01)	0.89
Midhigh				
Subcutaneous tissue area (cm <sup>2</sup> )	-0.154 (<0.005)	-0.232 (<0.005)	-0.245 (<0.005)	0.44
Non-subcutaneous tissue area (cm <sup>2</sup> )	0.064 (0.44)	-0.202 (0.01)	-0.086 (0.32)	0.07

\* P-value for comparing the slope to zero.

\*\* P-value for comparing the three slopes.

## RESULTS (cont'd)



NB: All P-values: Comparing each mean change or rate of change to zero.

## SUMMARY OF RESULTS

### MEAN CHANGES

- Positive
- Significantly different from zero
- Do not vary by strategy

### RATES OF CHANGE

- Subcutaneous tissue areas (3 sites)
  - Negative
  - Significantly different from zero
  - Do not vary by strategy

- Visceral area and non-subcutaneous tissue area of midarm
  - Positive
  - Significantly different from zero
  - Do not vary by strategy

- Non-subcutaneous tissue area of midhigh
  - Pattern inconclusive
  - Does not vary by strategy

## CONCLUSIONS

- Changes in the subcutaneous tissue areas and nonsubcutaneous tissue areas of the midarm and midhigh were able to be differentiated using anthropometric measures.
- Anthropometry provides a means of tracking changes in body composition over time.
- Anthropometry is a less costly and potentially far more widely available method for measurement of body composition than DXA, CT scan or MRI.

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