

Antiretroviral Therapy and the Longitudinal Assessment of Anthropometrics in the Multicenter AIDS Cohort Study

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Background:

Body shape changes are common among HIV-infected individuals receiving highly active antiretroviral therapy (HAART). It is unclear how body shape changes over time in HIV-infected individuals compared to HIV-seronegative controls and the extent that these changes are related to antiretroviral therapy.

Purpose:

To compare body shape changes over time in HIV-infected individuals with HIV-seronegative controls using simple anthropometric measures.

To determine the relationship between changes in body measurements and antiretroviral exposure.

Methods:

Study Population:

The Multicenter AIDS Cohort Study is an ongoing cohort of men who have sex with men (MSM), both HIV-infected and HIV-seronegative, initially enrolled in 1984. Since September 1999, circumference measurements of the waist, hip, thigh, and arm have been obtained at each semi-annual visit.

Outcome Measures:

- _ Body Mass Index (BMI)
- _ Waist:Hip Ratio
- _ Waist Circumference
- _ Thigh Circumference
- _ Hip Circumference
- _ Mid-Arm Circumference

All measurements were taken by trained personnel using the NHANES protocol.

Antiretroviral Exposure:

Exposure to antiretroviral therapy was assessed in two ways.

- First, HIV-infected subjects were divided into three therapy groups: 1) no antiretroviral therapy, 2) mono-therapy or non-HAART combination therapy, and 3) HAART. Therapy groups were updated at each semi-annual visit. Changes in anthropometrics were compared to the HIV-seronegative reference group.
- Second, the effect of cumulative exposure to each of the three major classes of antiretroviral therapy was determined.

Statistical Analysis:

The average change between 1999 and 2003 in each of the 6 outcome measures was estimated using mixed-effects regression models. Analyses were adjusted for age, nadir CD4 cell count, and BMI (for circumference measurements).

Results: Table 1 shows the baseline demographic characteristics of the cohort. Compared to the HIV-seronegative group, the HIV-infected groups were younger and had a lower BMI.

Table 1: Baseline Characteristics (1999)

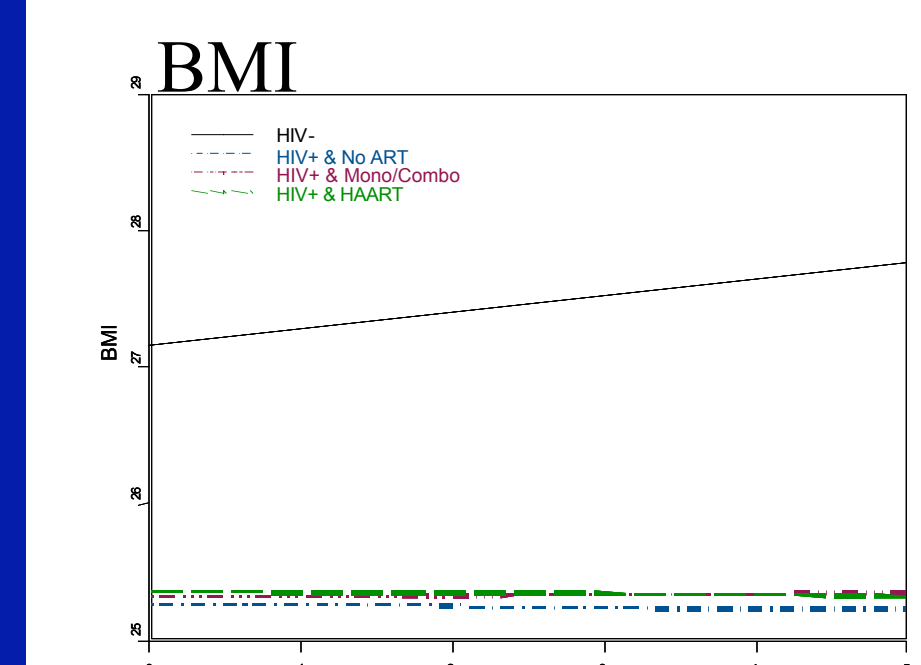
Characteristics (mean (std. dev.))	HIV- n=392	HIV+ & No ART n=94	HIV+ & Mono/Combo n=79	HIV+ & HAART n=488	P value
Caucasian (%)	334 (85%)	71 (76%)	61 (77%)	416 (85%)	0.0358
Years of age	48.3 (7.7)	45.9 (6.6)	46.3 (7.3)	45.6 (6.6)	<0.0001
Body mass index	27.3 (4.8)	25.5 (3.5)	25.3 (3.9)	25.3 (3.4)	<0.0001
Nadir CD4 cell count (cells/mm ³)	X	386.1 (221.3)	274.2 (171.7)	239.5 (165.3)	<0.0001
CD4 cell count (cells/mm ³)	X	492.6 (298.5)	489.9 (257.5)	503.2 (257.1)	<0.0001
HIV RNA (copies/ml)	X	48461.7 (91860.1)	17030.5 (84700.2)	12686.2 (70998.1)	0.0016

Analysis 1: Changes in Anthropometrics over time

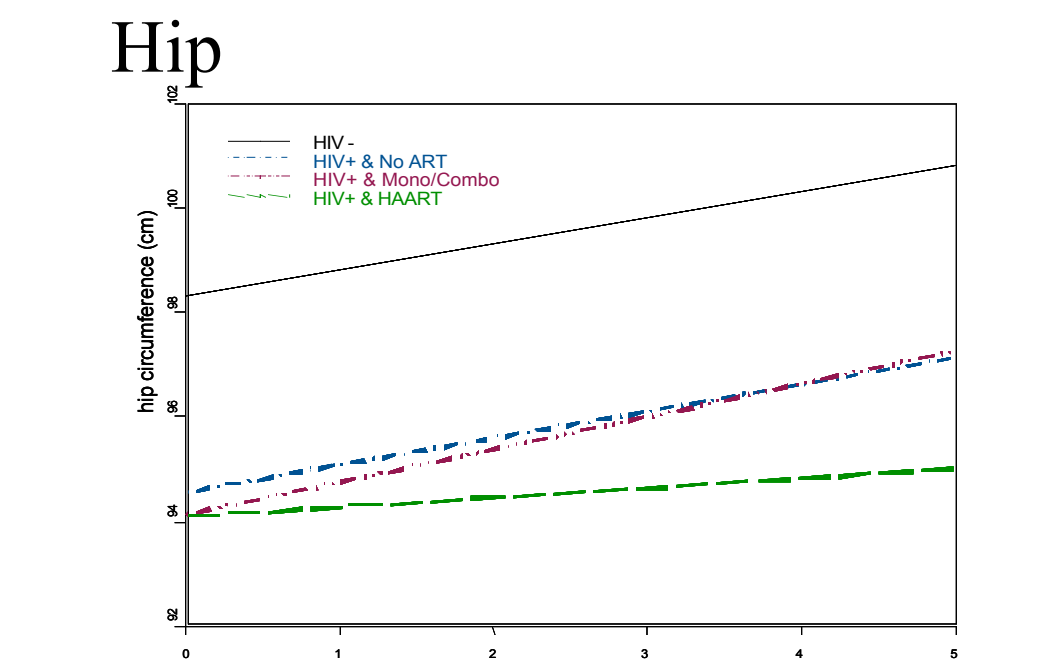
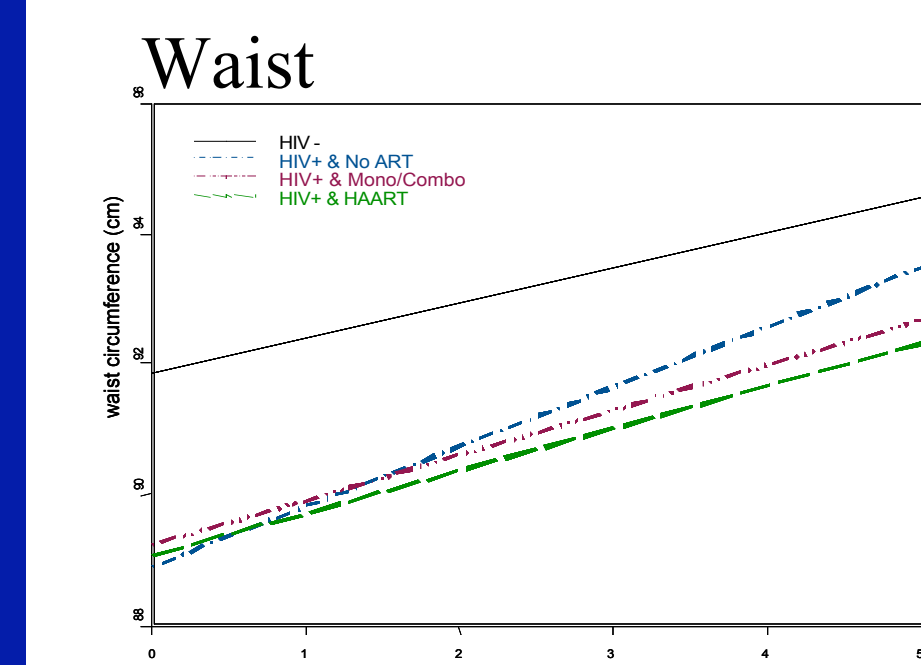
In this analysis, the HIV-infected men were divided into 3 groups. Table 2 shows the annual mean change in the 6 anthropometric outcomes. The HIV-infected groups are compared to the HIV-seronegative group. The average change over time is shown in the following figures.

Table 2: Annual Mean Change in 3 HIV+ Therapy Groups vs HIV- Controls

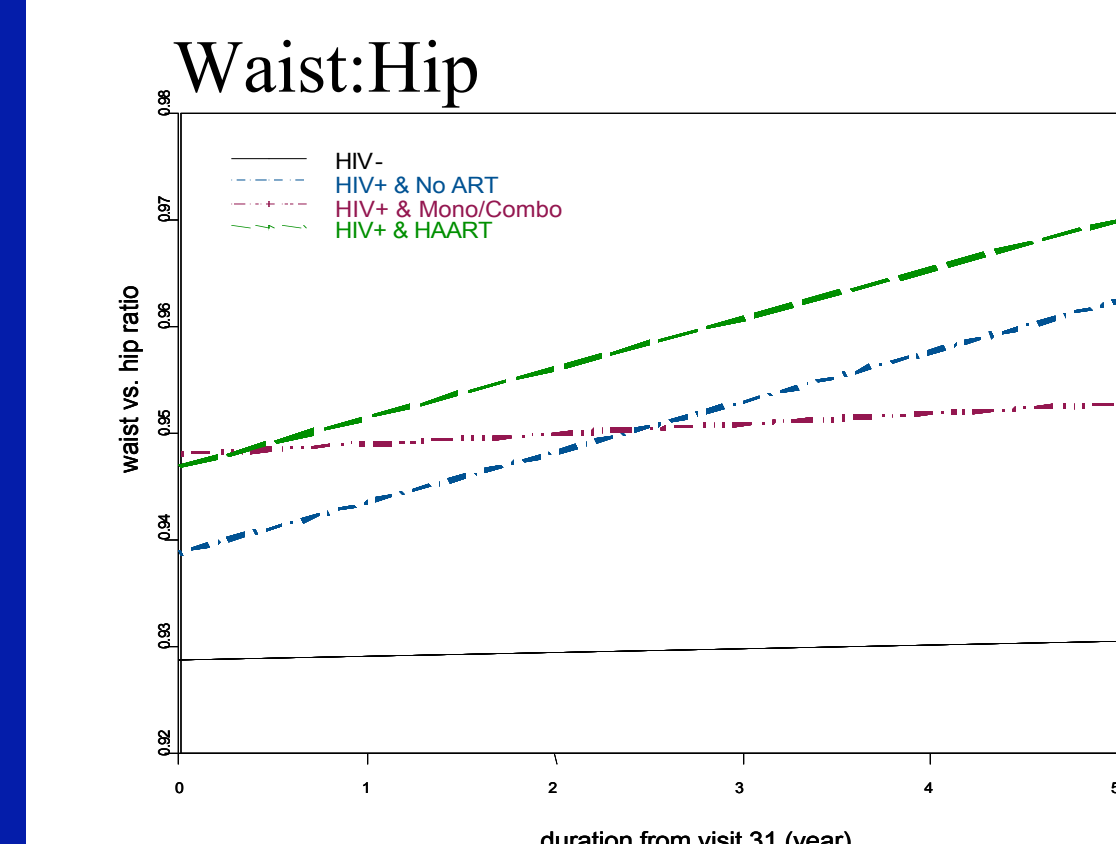
	HIV-			HIV+ & No ART			HIV+ & Mono/Combo			HIV+ & HAART		
	Est.	Std. Dev.	p	Est.	Std. Dev.	p	Est.	Std. Dev.	p	Est.	Std. Dev.	p
BMI (kg/m ² /yr)	0.121	0.035	<0.0001	-0.068	0.068	0.093	0.084	0.086	0.211	-0.066	0.032	<0.01
Waist (cm/yr)	0.545	0.092	0.916	0.185	0.072	0.689	0.235	0.566	0.647	0.085	0.415	
Hip (cm/yr)	0.493	0.065	0.513	0.138	0.097	0.626	0.179	0.487	0.182	0.061	<0.01	
Waist:Hip	0.0003	0.001	0.005	0.002	0.004	0.001	0.003	0.837	0.005	0.001	<0.01	
Arm (cm/yr)	0.045	0.039	0.084	0.079	0.063	0.036	0.102	0.931	0.024	0.036	0.679	
Thigh (cm/yr)	0.535	0.237	<0.001	0.420	0.063	0.036	0.542	0.399	-0.442	0.212	0.033	



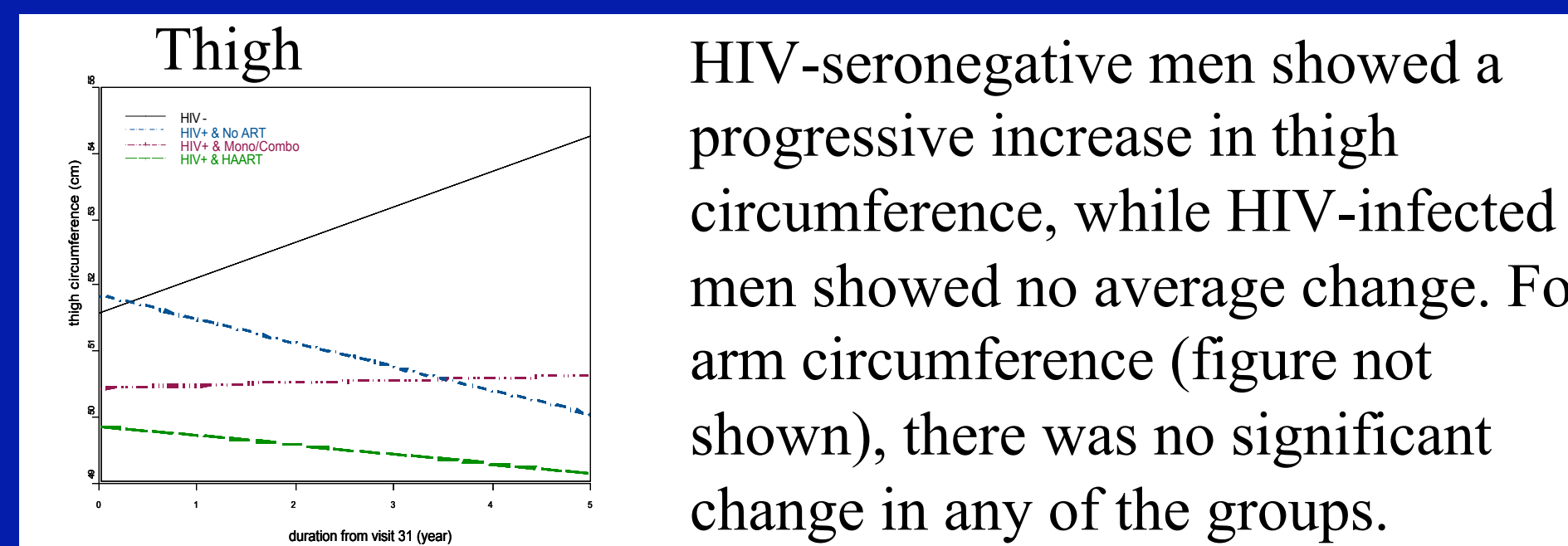
HIV-infected groups showed no average change in BMI over the study interval. By contrast, the HIV-seronegative controls showed a steady increase.



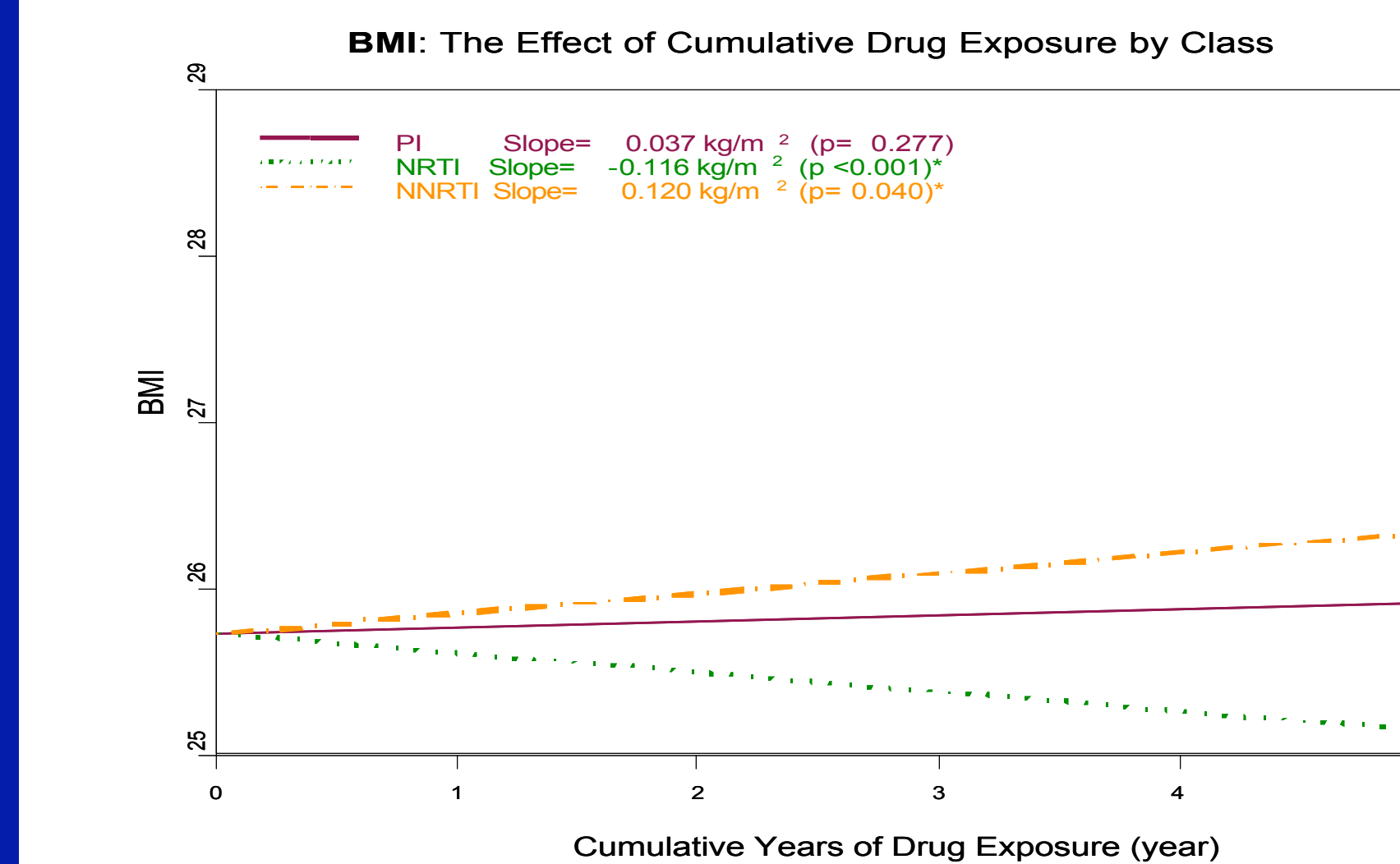
Despite baseline differences, each group of HIV-infected men had a similar rate of increase in waist circumference compared to the HIV-seronegatives. HIV-infected men receiving HAART had a slower rate of increase in hip circumference compared to the HIV-seronegative group.



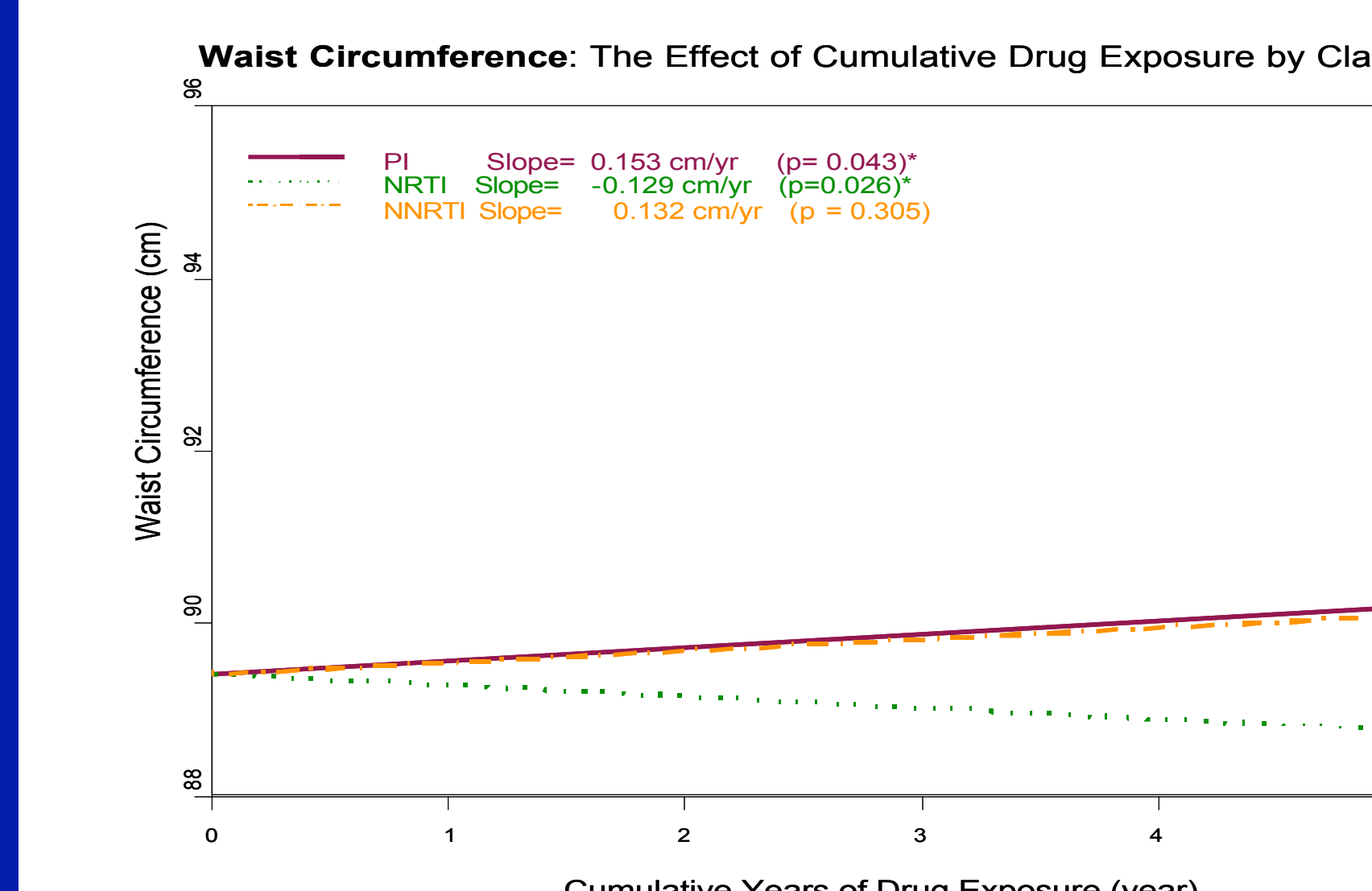
The difference accounted for the observed differences in change in the waist:hip ratio over time.



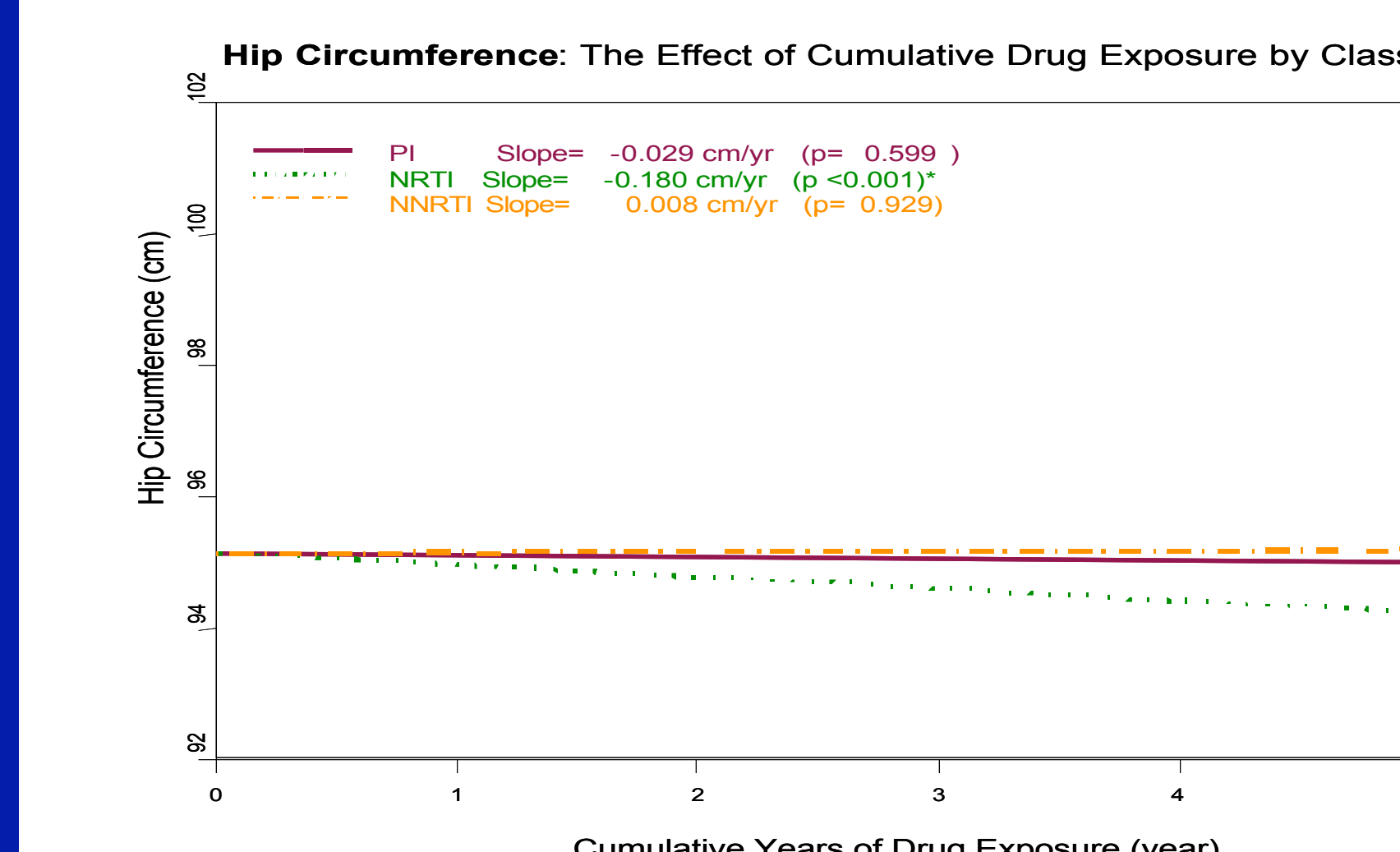
Analysis 2: Changes in anthropometrics with cumulative exposure to antiretroviral class



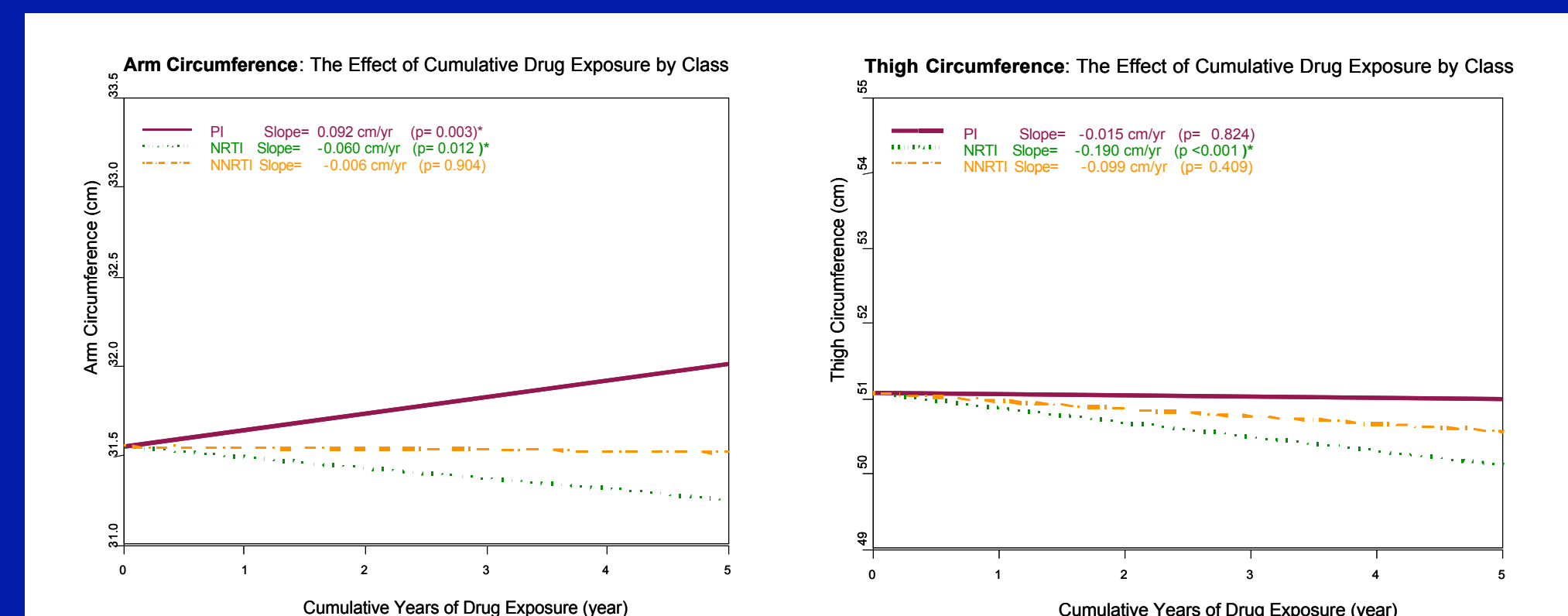
Each ARV class has differential effects on BMI. NRTIs are associated with a BMI decrease, NNRTIs with an increase, and PIs with a null effect.



Cumulative PI exposure was associated with increased waist circumference, whereas NRTI exposure was related to a significant decrease.



NRTI exposure was also associated with a significant decrease in hip circumference. None of the classes showed a significant effect on waist:hip ratio, but trends were seen for both NRTIs (0.001/year, p=0.06) and PIs (0.001/year, p=0.052).



In both the arms and thighs, cumulative NRTI exposure was associated with a significant decrease in circumference. PI exposure was related to an increase in arm circumference, but did not appear to affect thigh circumference. NNRTI exposure had no net effect on extremity circumference.

Summary:

- The increases in BMI over time observed HIV-seronegative group was not seen in the HIV-infected men. Cumulative NRTI exposure is associated with decreasing BMI in HIV-infected men.
- Waist circumference increased similarly in both the HIV-infected and the HIV-seronegative men. Among the HIV-infected men, PI exposure was related to increased waist circumference, whereas NRTI exposure was associated with a significant decrease.
- HIV-infected men on HAART did not show the increase in hip and leg circumference over time observed in the HIV-seronegative men. Decreases in hip and leg circumferences were strongly associated with cumulative NRTI exposure in HIV-infected men.

Conclusions:

- In this cohort of MSM, HIV-seronegative men had a greater increase in BMI, thigh and hip circumferences compared to the HIV-infected men on HAART over the 4 year interval. Interestingly, changes in waist circumference were similar in all groups.
- Cumulative exposure to PIs and NRTIs had differential and often opposing effects on anthropometric measures, underscoring their different contributions to morphologic changes associated with antiretroviral therapy.

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