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Body Mass Index and Waist Circumference of HIV-Infected Youth in a Miami Cohort: Comparison to Local and National Cohorts

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Abstract

Objective—Human immunodeficiency virus (HIV) infected youth are healthier due to effective antiretroviral therapies (ARVs). We compared anthropometric measurements and prevalence of overweight and obesity between perinatally-HIV-infected youth, a local HIV-uninfected comparison group and 2007–2010 National Health and Nutrition Examination Survey (NHANES) data. In addition, we compared only African American HIV-infected to NHANES African American.

Methods—Height, weight, body mass index (BMI) and waist circumference (WC) of HIV-infected youth, age 10–19 years, were compared among groups. BMI percentiles were categorized as underweight (< 5%), normal (5–<85%), overweight (85–<95%), and obese (≥ 95%). Clinical correlates were modeled as predictors of BMI and WC.

Results—134 HIV-infected (including 103 African Americans) (mean age 16.5y), 75 HIV-uninfected (mean age 14.2y), and 3216 NHANES (including 771 NHANES African Americans) (mean age 15.0y) youth were included in the analysis. Height and weight z-scores of HIV-infected were lower than HIV-uninfected and NHANES ($P = 0.056$). BMI, WC, and BMI category were not statistically different between groups. In the HIV-infected African American group, BMI z-score was lower (0.49 vs 0.76; $P = 0.04$) compared to NHANES African American. There were no significant predictors of BMI or WC for the HIV-infected group.

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Conflicts of Interest

The authors have no conflict of interest to disclose.

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Conclusion—HIV-infected children have similar BMIs and WCs as uninfected children both locally and nationally and show similar high rates of obesity and overweight. However, when compared to a more racially similar African American national sample, HIV-infected children have a lower BMI, suggesting that there may be persistent anthropometric differences in HIV.

Keywords

Human immunodeficiency virus; youth; obesity; body mass index; waist circumference

INTRODUCTION

Although the Human Immunodeficiency Virus (HIV) was known historically as a wasting disease,¹ the advent of highly active anti-retroviral therapy (HAART) has resulted in improved nutritional status among many HIV-infected persons, with a decreased overall prevalence of wasting in this population.² HIV has become a chronic disease, rather than one of progressive deterioration.

Obesity and lipodystrophy, the redistribution of body fat to the trunk and wasting of fat at the extremities, are some of the most obvious phenotypic cardiovascular risk factors for both HIV-infected adults and youth.^{3–5} Obesity and abdominal adiposity are serious health concerns for non-HIV-infected youth worldwide with an increase in their prevalence over the past several decades.^{6–10} HIV-infected youth may be particularly susceptible to the adverse sequelae of obesity and abdominal adiposity^{11,12} because of chronic inflammation and exposure to medications that can also affect cardiovascular disease risk. In turn, both obesity and abdominal adiposity are risk factors for diabetes, dyslipidemia, and cardiovascular disease in adults¹⁴ with evidence that these associations hold true in youth.^{15–17}

Sixty-nine percent of vertical transmission (i.e. mother-to-child transmission) of HIV occurs in African Americans, a race that is particularly susceptible to obesity and adiposity.^{18,7} Thus, in order to ascertain the prevalence of obesity and adiposity in HIV, it is prudent to compare HIV-infected youth not only to national standards but also to demographically-similar populations. The extent to which HIV-infected youth follow national and international trends for obesity and abdominal adiposity has not been well reported.

The objectives of our study are to compare BMI, the prevalence of overweight and obesity, and waist circumference of a cohort of youth with perinatally-acquired HIV to a local cohort of youth without HIV and to the general US population based on the NHANES data on BMI and waist circumference for the years 2007–2010. In a subset analysis, we compared HIV-infected African Americans to an African American subset of NHANES. We also determined if clinical factors such as race; HIV Center for Disease Control (CDC) stage; viral load; CD4 count; HAART, protease inhibitor (PI), nucleoside reverse transcriptase inhibitor (NRTI), and non-nucleoside reverse transcriptase inhibitor (NNRTI) duration are associated with BMI or waist circumference in our HIV cohort.

MATERIALS AND METHODS

Study Population

HIV-infected subjects followed in the Pediatric Special Immunology Program at the University of Miami, Miami, FL were enrolled in a National Heart, Lung, and Blood Institute sponsored longitudinal cohort study that evaluated cardiovascular disease risk in perinatal HIV-infected youth between August 2004 and March 2011. HIV infection was confirmed by repeatedly positive serum enzyme-linked immunosorbent assays and western blot assays, repeatedly positive HIV RNA or DNA polymerase chain reaction (PCR) assays, or by HIV culture. All of these laboratory tests were done in outpatient laboratories that were determined based on clinical care.

A total of 165 HIV-infected children and adolescents aged 10 to 19 years were seen in the Special Immunology clinic in 2010. For this cross-sectional analysis, the most recent visit between 2007 and 2010 with complete anthropometric data (HIV-infected and HIV-uninfected) was used and constituted the dataset of 134 individuals. HIV-infected youth who did not acquire HIV from their mother (e.g horizontally-infected) were excluded, as were those who were wheelchair-bound since anthropometric data could not be accurately obtained on these individuals.

The HIV-uninfected comparison group was a convenience group of 75 uninfected youth. These youth were identified from the family members of the HIV-infected group or from an urban general pediatric outpatient program at the University of Miami that cares for youth of similar socioeconomic backgrounds. None of these individuals were known to be HIV-infected. Uninfected individuals were excluded if they had any chronic illness or an acute infectious process.

The NHANES database¹⁹ was used as an additional comparison group of children and adolescents. NHANES is a series of studies to assess the health and nutritional status of children and adults in the United States. Its data, including anthropometric measurements, is reported on a biannual basis. The NHANES uses probability sampling and weighting methodology.²⁰ Ignoring its complex design can lead to biased population estimates and overstated significance levels. Thus, the current study followed NHANES guidelines²⁰ to account for the design features, including stratification, cluster sampling, and weighting. Demographic and anthropometric data were extracted from the NHANES database for the years 2007–2008 and 2009–2010 for all individuals ages 10 to 19 for a total of 3216 individuals as representative of a national sample of children and adolescents of this age group. We also identified a subset of 771 African American NHANES participants to compare anthropometrics to an African American HIV cohort.

The Human Subjects Research Office at the University of Miami approved the research protocol (protocol number 20030814), and written informed consent from the parent or guardian and assent from the patient (when appropriate) were obtained.

Data Collection

At the visit, the following clinical data were collected for both the HIV-infected group and HIV-uninfected group: demographic information (age, sex, race), weight, height, and waist circumference. For the HIV-infected group only, Tanner stage; CDC HIV stage;²¹ CD4 T-lymphocyte count; HIV viral load; and highly active antiretroviral (HAART), PI, NRTI, and NNRTI current use and lifetime duration were obtained. The definition of HAART was guided by the DHHS/Kaiser Panel [DHHS/Kaiser 2004] guidelines and defined as: (a) two or more NRTIs in combination with at least one PI or one NNRTI; (b) one NRTI in combination with at least one PI and at least one NNRTI; (c) a regimen containing ritonavir and saquinavir in combination with one NRTI and no NNRTIs; or (d) an abacavir or tenofovir containing regimen of three or more NRTIs in the absence of both PIs and NNRTIs, except for the three-NRTI regimens consisting of: abacavir + tenofovir + lamivudine OR didanosine + tenofovir + lamivudine.²² If CD4 count or viral load were not collected at the most recent visit, a value within 90 days of the visit was used.

Weight and standing height were measured by standardized procedures.²³ BMI was calculated as weight (kg)/height² (m²).²⁴ Waist circumference was measured using a non-stretchable plastic tape measure at the navel at the end of gentle exhalation.²³ Weight, height and BMI were standardized for age and sex using CDC-derived percentages and z-scores.²⁴ Each child was classified as underweight (BMI<5%), normal weight (5%–<85%), overweight (85%–<95%) or obese (>95%).²⁵

Statistical Analysis

We used linear mixed models with random family cluster-specific intercepts and heterogeneous residual variances for the HIV-infected and HIV-uninfected groups to determine if any differences in height/height z-score, weight/weight z-score, BMI/BMI z-score, or waist circumference existed between our HIV-infected group and our HIV-uninfected group. Height, weight, BMI z-score, and waist circumference of the NHANES sample and NHANES African American subsample were also compared to our HIV-infected population using Welch's t-tests.

In a sub-analysis using only HIV-infected children, race; CD4 count; viral load; HIV CDC stage; and HAART, PI, NRTI, and NNRTI duration were modeled as predictors of BMI z-score in linear mixed models with random family cluster-specific intercepts. In a separate random intercept model, race; sex; age; CD4 count; viral load; HIV CDC stage; and HAART, PI, NRTI, and NNRTI duration were modeled as predictors of waist circumference. Tanner stage was included in a separate analysis as a predictor of BMI z-score and waist circumference because 27% of Tanner stage data was missing from the sample.

Although primarily for descriptive purposes, a categorical analysis of BMI and HIV status was also performed. This was done to provide additional information regarding possible clinical interpretations. BMI categories were compared between the HIV-infected and HIV-uninfected groups using the Cochran-Armitage test. Categories were compared between HIV and NHANES using a chi-square test.

Statistical analyses were performed with the SAS statistical software program, version 9.3 (SAS Institute, Cary, NC).

RESULTS

A total of 134 HIV-infected (including 103 African Americans), 75 HIV-uninfected, and 3216 NHANES (including 771 NHANES African American) children and adolescents were included in the analysis. HIV-specific characteristics of our affected population are shown in Table 1. Thirty-seven percent of the group met criteria for the Acquired Immunodeficiency Syndrome (AIDS) (CDC class C). The median CD4 count was 535 cells/mm³ and 20% of the HIV-infected population had a CD4 count less than 200 cells/mm³. The median viral load was 760 copies/mL with 42% having an undetectable viral load (<400 copies/mL). Ninety percent of children were on a highly active antiretroviral therapy (HAART) regimen with a median duration of 110 months. Ninety three percent of the youth on HAART had a PI as part of their HAART regimen.

Table 2 compares the demographic and anthropometric characteristics of the HIV-infected and HIV-uninfected groups. The HIV-infected group was older than the HIV-uninfected group (16.5 years versus 14.2 years; $P<0.0001$) and was more likely to be African American (77% versus 52%; $P=0.002$). After adjusting for race and accounting for biological relatedness, the HIV-infected group was shorter than the HIV-uninfected group (height z-score -0.41 versus 0.10 ; $P=0.003$) and although not statistically significant, BMI z-score was lower in the HIV-infected group as well (0.69 versus 0.87 ; $P=0.36$). Waist circumference--adjusted for age, sex, and race, and accounted for biological relatedness--was not statistically significantly different between the HIV-infected and HIV-uninfected group (81.9 cm versus 80.5 cm; $P=0.66$).

Table 3 compares the demographic and anthropometric characteristics of the HIV-infected group and the NHANES sample. All anthropometric data were unadjusted except for z-score data, which was intrinsically adjusted for age and gender, and waist circumference, which was adjusted for age and sex. The HIV-infected group was older than NHANES (16.5 years versus 15.0 years, $P<0.001$). Compared to NHANES, the HIV-infected group was shorter (height z-score -0.48 versus 0.19 , $P<0.001$) and lighter (weight z-score 0.27 versus 0.59 , $P=0.01$). The HIV-infected group had non-statistically significant differences in BMI z-scores ($P=0.84$). Waist circumference was not statistically significantly different ($P=0.63$).

Table 4 compares the demographic and anthropometric characteristics of the African American HIV-infected group and the African American NHANES subgroup. Similar to the racially diverse comparison, the African American HIV-infected group was older (16.4 years versus 15.0 years, $P<0.001$), shorter (height z-score -0.44 versus 0.24 , $P<0.001$), and lighter (weight z-score 0.26 versus 0.82 , $P<0.001$) than NHANES African American. However, the HIV-infected group had a statistically significant difference in BMI z-score ($P=0.04$). Waist circumference was not statistically significantly different ($P=0.96$, adjusted for age and sex).

Figure 1 shows the frequency of individuals in each sample categorized as underweight, normal, overweight, and obese. For the HIV-infected group, 13.4% were overweight compared to 10.7% in the HIV-uninfected group and 15.6% in the NHANES sample. Twenty-two percent of the HIV-infected group was obese compared to 32.0% in the HIV-uninfected group and 20.1% in the NHANES sample. There were no statistically significant differences in BMI categories between the HIV-infected and HIV-uninfected groups, the NHANES sample, and NHANES African American ($P>0.08$). However, there was a trend that the HIV-infected group had lower rates of overweight and obesity when compared to the NHANES African American sample (13.4% vs 16% overweight and 22% vs 26% obese, respectively).

Among the HIV-infected group alone, we examined factors associated with a higher BMI. In a random intercept linear model analysis, there were no statistically significant associations (all P -values >0.14) between race, HIV CDC stage, CD4 count, viral load, and duration of HAART and BMI z-score. In a separate random intercept linear model analysis with waist circumference as the outcome and age and gender added in the model as predictors, age was a statistically significant predictor ($P = 0.046$) of waist circumference but the other covariates were not (all P -values >0.19). A similar model using individual antiretroviral drug classes (i.e. PI, NRTI, and NNRTI) instead of HAART in the model showed no associations with BMI z-score ($P>0.15$). Again, age was a statistically significant predictor ($P=0.03$) of waist circumference but the other covariates were not (all P -values >0.20). When Tanner stage was included as a predictor of both BMI and waist circumference, there were no statistically significant associations.

DISCUSSION

Our study shows differences in some anthropometric measures (heights and weights) among HIV-infected youth when compared to a local, uninfected group or to a multiethnic national sample of youth of similar ages. BMI z-scores and waist circumferences are similar, suggesting comparable rates of “adiposity” between these groups. Yet when these measures are compared between an exclusively African Americans subset of HIV-infected and African American NHANES, there are even greater differences in height and weight and significantly lower BMI z-scores in HIV-infected youth. When BMI is categorized, we find that about 35% of the HIV-infected youth meet criteria for overweight or obese. These percentages are similar to our contemporary group of uninfected youth and to national trends,^{7–8} yet lower than the national African American sub-sample (42%). We found that HIV-specific factors were not associated with BMI or waist circumference.

Advances in antiretroviral therapy have led to improvements in growth of HIV-infected youth^{2,26–29} yet our data show that these youth still lag behind their racially-matched peers in some anthropometric parameters. In essence, HIV-infected youth are “less obese” than their non-infected counterparts, but still plot along “normal” anthropometric measures. Some studies find lower BMIs in HIV-infected children compared with demographically similar uninfected children exposed to HIV in utero.^{26,31} Rates of obesity in children and adolescents differ by race, with African Americans reported to have higher rates of obesity than non-Hispanic whites.⁷ Our analyses show these differences as the BMI of the African

American subsample of NHANES was higher than the BMI of the entire NHANES sample (BMI z-score 0.49 vs 0.76). Therefore, despite improvements in growth with antiretroviral therapy and better viral control, HIV-infected youth continue to demonstrate lower anthropometric parameters when compared to a demographically similar group.

Approximately 33.2% of United States HIV-uninfected children and adolescents aged 6–19 years are either overweight or obese.⁸ The prevalence of overweight and obesity in our HIV-infected population is similar to national trends, with 35.8% being overweight or obese. For the African American NHANES sample, 42.5% are overweight or obese. Although the difference in BMI categories between HIV-infected and NHANES African American does not reach statistical significance, our HIV-infected group has a lower prevalence of overweight and obesity compared to a racially similar national sample of NHANES African Americans ($P=0.08$). These categorical findings further support the need to compare HIV-infected youth to a group with a similar racial composition.

The differences in BMI between HIV-infected and uninfected African Americans could possibly be a result of persistent inflammation associated with chronic viral infection,^{32,33} as other disorders associated with chronic inflammation can affect growth in children.^{34–36} High viral load and antiretroviral medications^{32,33} are associated with chronic inflammation as manifested by higher levels of biomarkers of inflammation in children with HIV infection compared to controls^{32,37} that can, in turn, affect basal metabolic rate.³⁸ Our study did not find an association between measures of HIV disease severity (CDC stage, viral load, CD4 counts) and anthropometric outcomes. However, there are data that also show persistent inflammation in the context of good HIV viral control.³⁹ Studies also demonstrate that the anthropometric effects of HIV are apparent even *in utero* where infants prenatally exposed to HIV but who were uninfected have lower birth lengths and weights compared with unexposed infants.^{40,41}

Although our data support a lower BMI in HIV-infected youth compared to their uninfected, racially alike peers, there is a high prevalence of obesity in these individuals. HIV-infected youth are invariably exposed to many of the same risks for overweight and obesity that are relevant to the general population. Low cardiorespiratory fitness⁴² and dietary patterns that are more obesogenic are reported in HIV-infected youth.⁴³ These lifestyle factors can contribute to high rates of overweight and obesity in HIV-infected children. Obesity⁴⁴ and HIV infection^{4,45} are known independent risk factors for cardiovascular disease. Thus although these youth may be “less obese” than their peers, the high prevalence of obesity that still exists in these individuals and higher risk of cardiovascular disease due to the virus make HIV-infection in youth a public health concern.

There are limitations to our study. We did not have a perfectly matched control group. Our HIV population was drawn from a convenience sample of HIV-infected youth seen at our institution. Our comparison group consisted of youth who were either family members of our HIV-infected cohort or who were recruited from a nearby urban pediatric practice with an ethnically and socio-economically similar population. This comparison population was younger than our sample population, had a smaller percentage of African Americans (52% vs 77% in HIV-infected), and many were related to our HIV-infected group. Although we

controlled for these factors in our analyses, this mismatch could affect our results. It is possible that a greater sample size in our local HIV-uninfected group could have resulted in better power to determine differences between the groups. In addition, one covariate that we were unable to control for in our studies is pubertal stage since this data was lacking in our uninfected comparison group and NHANES sample. Differences in Tanner stage between groups could influence BMI and waist circumference and affect the results.

In conclusion, we found that HIV-infected youth's BMI and waist circumference approximate those of a nationally representative sample. However, there may be more subtle differences in BMI when HIV-infected youth are compared to demographically similar populations. We found that HIV-specific factors such as HIV CDC stage, viral load, CD4 count, and HAART, PI, NRTI and NNRTI duration were not associated with BMI or waist circumference in HIV-infected youth. Future studies should try to define factors that are associated with residual anthropometric differences in demographically matched HIV-infected youth as well as to determine effective interventions that can target those youth who are overweight and obese and who parallel national trends in obesity and carry additional risks for cardiometabolic disease.

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Figure 1.

BMI categories of 134 HIV-infected youth, 75 HIV-uninfected youth, 3216 2007–2010 NHANES sample, and 771 2007–2010 NHANES subsample of African Americans. No statistically significant differences across BMI categories were observed. HIV-infected vs HIV-uninfected, $P=0.20$; HIV-infected vs NHANES, $P=0.63$; HIV-infected vs NHANES African Americans, $P=0.08$.

Table 1**HIV-Specific Characteristics of 134 HIV-Infected Youth**

Variable	
CDC stage, n, (%)	
Stage N	10 (7)
Stage A	26 (19)
Stage B	49 (37)
Stage C	49 (37)
CD4 count (cells/mm³), median (IQR)	535 (235,800)
CD4 category, n, (%)	
<200	27 (20)
200–500	33 (25)
>500	70 (52)
Not available	4 (3)
Viral load (copies/mL), median (IQR)	760 (176, 5908)
Viral load category, n, (%)	
<400	56 (42)
400–5000	41 (31)
>5000	35 (26)
Not available	2 (1)
Antiretroviral Therapy	
Number currently taking medication class, n, (%)	
NRTI	119 (89)
PI	109 (81)
NNRTI	22 (16)
HAART	120 (90)
with PI	112 (93)
without PI	8 (7)
Medication lifetime duration (months), median (IQR)	
NRTI	139 (95–178)
PI	98 (36–124)
NNRTI	29 (0–75)
THAART	110 (75–131)

HIV=human immunodeficiency virus, CDC=Center for Disease Control, HAART=highly active anti-retroviral therapy, NRTI=nucleoside reverse transcriptase inhibitor, NNRTI=non-nucleoside reverse transcriptase inhibitor, PI=protease inhibitor, IQR=interquartile range

Table 2

Characteristics of 134 HIV-infected and 75 HIV-uninfected Infected Youth

Variable	HIV-infected	HIV-uninfected infected ¹	P-value
Demographics			
Age (y), mean (SE)	16.5 (0.25)	14.2 (0.31)	<0.0001 ²
Male, n (%)	64 (48)	40 (53)	0.47 ²
Race, n (%) ³	--	--	0.002 ²
African-American	103 (77)	39 (52)	--
Hispanic	27 (20)	28 (37)	--
White/other	4 (3)	6 (8)	--
Missing	0 (0)	2 (3)	--
Anthropometrics – estimated mean (SE)			
Height (cm)	161.3 (0.87)	160.1 (1.50)	0.48
Height z-score ⁴	-0.41 (0.16)	0.10 (0.17)	0.003
Weight (kg)	63.6 (1.72)	63.1 (2.66)	0.88
Weight z-score ⁴	0.48 (0.20)	0.89 (0.21)	0.056
BMI (kg/m ²)	24.1 (0.55)	24.3 (0.94)	0.88
BMI z-score ⁴	0.69 (0.18)	0.87 (0.20)	0.36
WC (cm) ⁵	81.9 (2.77)	80.5 (3.54)	0.66

¹ Of the 75 non-infected participants, 25 were biologically related to an HIV-infected participant. Biological relatedness has been accounted for in these comparisons via linear mixed models with random family cluster-specific intercepts. In addition to random intercepts, the linear mixed models also included heterogeneous residual variances for the HIV-infected and HIV-uninfected groups.

² p-value based on Fisher's exact test

³ The four HIV-infected and three HIV-uninfected black Hispanics in this study are classified as Hispanic in the demographic information and in the analyses.

⁴ Adjusted for race and biological relatedness

⁵ Adjusted for sex, age, race and biological relatedness; 13/134 HIV+ and 35/75 non-infected did not have WC data.

WC= waist circumference

Table 3

Characteristics of 134 HIV-infected Youth and 3216 NHANES

Variable	HIV-infected	NHANES	P-value ¹ (HIV vs NHANES)
Demographics			
Age (y), mean (SE)	16.5 (0.25)	15.0 (0.06)	<0.001
Male, n (%)	64 (48)	52	0.36
Race, n (%)	--	--	<0.001
African American,	103 (77)	482 (15)	--
White/other, n (%)	4 (3)	2123 (66)	--
Hispanic, n (%)	27 (20)	611 (19)	--
Anthropometrics-mean (SE)			
Height (cm)	161.4 (0.87)	162.6 (0.37)	0.21
Height z-score	-0.48 (0.10)	0.19 (0.03)	<0.001
Weight (kg)	63.26 (1.68)	61.6 (0.54)	0.36
Weight z-score	0.27 (0.12)	0.59 (0.03)	0.01
BMI (kg/m ²)	24.05 (0.54)	22.92 (0.14)	0.04
BMI z-score	0.51 (0.11)	0.53 (0.03)	0.84
WC (cm) ²	79.93 (1.36)	79.25 (0.35)	0.63

¹ p-value based on Welch's unpaired t-test for continuous variables and Fisher's exact test for categorical variables.

² adjusted for sex and age; 13/134 HIV+ and 28/3216 NHANES did not have WC data.

WC=waist circumference

Table 4

Characteristics of 103 African-American HIV-infected Youth and 771 African-American NHANES

Variable	HIV-infected AA	NHANES AA	P-value ^I
Demographics			
Age (y), mean (SE)	16.4 (0.30)	15.0 (0.12)	<0.001
Male, n (%)	52 (50)	397 (51)	0.45
Anthropometrics-mean (SE)			
Height (cm)	161.4 (0.96)	163.2 (0.46)	0.10
Height z-score	-0.44 (0.12)	0.24 (0.04)	<0.001
Weight (kg)	63.12 (1.98)	65.65 (0.82)	0.24
Weight z-score	0.26 (0.14)	0.82 (0.04)	<0.001
BMI (kg/m ²)	24.00 (0.64)	24.25 (0.25)	0.72
BMI z-score	0.49 (0.12)	0.76 (0.04)	0.04
WC (cm) ²	78.9 (1.56)	78.8 (0.51)	0.96

^I p-value based on Welch's unpaired t-test for continuous variables and Fisher's exact test for categorical variables.

² adjusted for sex and age; 8/103 HIV+ African-American and 9/771 NHANES African-American did not have WC data.

WC=waist circumference