Short Communication

From Wasting to Obesity: Initial Antiretroviral Therapy and Weight Gain in HIV-Infected Persons

Wanda Lakey,^{1,2} Lan-Yan Yang,³ William Yancy,^{2,4} Shein-Chung Chow,³ and Charles Hicks⁵

Abstract

Data on weight gain and the progression to overweight/obesity in HIV-infected persons during initial combination antiretroviral therapy (cART) are limited, and comparisons to the general population are inconclusive. Weight and body mass index (BMI) changes were studied in HIV-infected adults who remained on initial cART for 12 consecutive months and in an HIV-uninfected cohort receiving care at Duke University Medical Center between 1998 and 2008. Overweight/obesity was defined as BMI ≥ 25 kg/m². Variables were analyzed by Chi-square and Student's *t*-tests. Ninety-two HIV-infected persons (median age 38.2 years) met inclusion criteria. Weight and BMI increased during 12 months of cART (80.0 to 84.4 kg, $p < 0.0001$; 26.4 to 27.9 kg/m², $p < 0.0001$; respectively). Weight gain was greater in HIV-infected females compared to males (8.6 vs. 3.6 kg, $p = 0.04$), in persons treated with protease inhibitor (PI)-based cART compared to non-PI-based cART (9.0 vs. 2.7 kg, $p = 0.001$), and in persons with a pretreatment CD4 count < 200 cells/mm³ compared to ≥ 200 cells/mm³ (8.9 vs. 0.3 kg, $p < 0.0001$). Overweight/obesity prevalence increased from 52% to 66% during 12 months of initial cART, a 27% relative increase ($p = 0.002$). HIV-infected persons had a lower prevalence of pretreatment overweight/obesity compared to 94 age-matched control subjects (52% vs. 91%, $p < 0.001$); however, there was no change in weight (92.7 vs. 93.0 kg, $p = 0.5$) or overweight/obesity prevalence (91% to 92%, $p > 0.9$) during 12 months in the control cohort. Management should anticipate excess weight gain during the first year of cART in persons who are female, have a pretreatment CD4 < 200 cells/mm³, or will initiate PI-based cART.

EMERGING EVIDENCE FROM restricted patient samples suggests a high prevalence of overweight and obese adults in the HIV-infected population, albeit with similar or lower prevalence rates compared to an uninfected population.^{1,2} It remains uncertain, however, if a high rate of obesity occurs in diverse HIV-infected populations, or how the weight trajectory of HIV-infected populations compares to the general population. Additionally, the role of initial combination antiretroviral therapy (cART) in obesity remains unanswered. Changes in weight occurring after first time initiation of cART may be particularly important in the overall rates of obesity among HIV-infected persons.

Obesity increases all-cause mortality and the risk of morbidity from diabetes, hypertension, hyperlipidemia, and cardiovascular disease (CVD) in the general population.³ One incompletely explored risk factor for CVD in HIV-in-

fectured persons is cART-induced obesity. The frequency of CVD in HIV-infected persons has increased, at least in part due to prolonged survival from cART.⁴⁻⁶ Although the reasons for increased HIV-associated CVD risk are not fully understood, cART may be a potential factor. Previous data showed a 26% relative increase in the rate of myocardial infarction (MI) per year of exposure to cART.⁶ The Framingham CVD risk-prediction model used in the general population underestimates the risk of MI in HIV-infected persons receiving cART, perhaps due to unmeasured risk factors such as obesity.⁷ Additional longitudinal data on progression to obesity during cART are needed to establish obesity as an emerging chronic medical condition among HIV-infected persons.

To improve the understanding of weight gain linked to initial cART use, we designed a longitudinal cohort study to

¹Department of Internal Medicine, Division of Endocrinology, Diabetes, and Metabolism, Duke University Medical Center, Durham, North Carolina.

²Department of Internal Medicine, Durham Veterans Affairs Medical Center, Durham, North Carolina.

³Department of Biostatistics and Bioinformatics, Duke University School of Medicine, Durham, North Carolina.

⁴Department of Internal Medicine, Division of General Internal Medicine, Duke University Medical Center, Durham, North Carolina.

⁵Department of Internal Medicine, Division of Infectious Diseases, Duke University Medical Center, Durham, North Carolina.

establish the prevalence of overweight and obesity in a diverse HIV-infected adult population receiving care at Duke University Medical Center. The prevalence of overweight and obesity in the HIV-infected cohort was compared to an HIV-uninfected control group receiving care at primary care clinics affiliated with Duke University Medical Center.

Subjects were chosen consecutively from the Duke AIDS Research and Treatment Center database, which encompasses HIV-infected patients throughout North Carolina and surrounding states. Data from the pretreatment visit were recorded in HIV-infected treatment-naïve adults (≥ 18 years of age) who remained on initial cART for at least 12 consecutive months between 1998 and 2008. Drug substitutions within the same class of drug were allowed if toxicity occurred. Available data on height and weight from ± 70 days of the pretreatment visit and after 12 months of cART were inclusion criteria. Exclusion criteria included any of the following conditions associated with weight gain or loss within 6 months of the study period: pregnancy, malignancy (other than squamous or basal cell carcinoma of the skin), newly diagnosed or unstable thyroid disorder, use of megestrol or dronabinol, ≥ 1 month prednisone (≥ 5 mg or equivalent dose of another glucocorticoid), androgenic steroid use, history of diabetes or use of glucose-lowering agents, use of specific psychiatric or anticonvulsant agents (thioridazine, olanzapine, clozapine, quetiapine, risperidone, lithium, mirtazapine, paroxetine, valproic acid, carbamazepine, gabapentin), concurrent treatment of hepatitis C, diagnosis of a new opportunistic infection as defined by the Centers for Disease Control during cART use, congestive heart failure treated with diuretic therapy, and hemodialysis.

An online query system with repository data from operational systems serving Duke University Medical Center's hospitals identified the control group. Adult subjects (≥ 18 years of age), followed in primary care clinics between 1998 and 2008, were identified and matched for age with the HIV-infected cohort. Control subjects with baseline height, baseline weight, and weight from a primary care visit within 12 months ± 70 days from the baseline visit were included. Exclusion criteria from the HIV-infected cohort were also used for the control group.

Data were abstracted from ± 70 days of the pretreatment visit and 12 months after cART initiation in the HIV-infected cohort and ± 70 days of the baseline visit and after 12 months of follow-up in the control cohort. BMI, expressed as weight (kg)/[height (m)]², was calculated using the recorded weight and height. Body mass index (BMI) (kg/m²) categories were defined as follows: underweight < 18.50 , normal 18.50–24.99, overweight 25.00–29.99, obese ≥ 30.00 , overweight/obese ≥ 25.00 .³ Race, gender, medical history, and medication use were abstracted from the medical record. CD4 cell counts and HIV RNA viral load measurements were recorded ± 70 days of the pretreatment and 12-month clinic visits. Glucose and lipid panel tests were recorded, if available, without regard to fasting. Hypertension was diagnosed if any of the following criteria were present: documented in the medical record, use of antihypertensive medication for this purpose, or ≥ 2 average systolic or diastolic blood pressures were $> 140/90$. Dyslipidemia was diagnosed if any of the following criteria were present: documented in the medical record, use of lipid-lowering medication, total cholesterol > 240 mg/dl, HDL-cholesterol < 40 mg/dl,

TABLE 1. BASELINE CHARACTERISTICS OF HIV-INFECTED PERSONS PRIOR TO INITIAL COMBINATION ANTIRETROVIRAL THERAPY AND CONTROL COHORT AT STUDY INCLUSION

Category	HIV-infected (n = 92)	Control (n = 94)	p-value
Age (years)	38.2 $\pm$ 10.5	38.6 $\pm$ 4.2	0.8
Gender			
Female	15 (16%)	49 (52%)	<0.0001
Male	77 (84%)	45 (48%)	
Race/ethnicity			
AA	48 (52%)	78 (83%)	<0.0001
Non-AA	44 (48%)	16 (17%)	
Insurance			
Medicaid	10 (11%)	15 (16%)	0.3
Non-Medicaid	82 (89%)	79 (84%)	
Year of cART initiation/study inclusion			
1998–2004	48 (52%)	9 (10%)	<0.0001
2005–2008	44 (48%)	85 (90%)	
Weight (kg)	80.0 $\pm$ 19.4	92.7 $\pm$ 19.7	<0.0001
BMI (kg/m ²)	26.4 $\pm$ 6.8	31.9 $\pm$ 6.9	<0.0001
CD4 count (cells/mm ³)	219.3 $\pm$ 181.0	—	—
CD4 < 200	44 (48%)		
CD4 ≥ 200	48 (52%)		
HIV RNA viral load (copies/ml)	633,963.8 $\pm$ 1,863,934.1	—	—
Initial cART regimen			
PI-Based	25 (27%)	—	—
Non-PI-based	67 (73%)		

Data for age, weight, BMI, CD4 count, and HIV RNA viral load presented as mean $\pm$ standard deviation.

AA, African-American; BMI, body mass index; cART, combination antiretroviral therapy; PI, protease inhibitor.

or non-HDL-cholesterol >190 mg/dl. New-onset diabetes was diagnosed if documented in the medical record, hemoglobin A_{1c} $\geq 6.5\%$, or if a glucose-lowering agent was initiated. New coronary or cerebrovascular disease was diagnosed if recorded in the medical record.

Continuous data were compared using a Student's *t*-test. Changes in weight were analyzed by a paired Student's *t*-test within a cohort and by a Student's *t*-test between the two cohorts. Categorical data were compared using Chi-square statistics. Statistical analyses were performed using SAS, version 9.2 (SAS Institute; Cary, NC).

Ninety-two HIV-infected and 94 control subjects with complete data were identified. Baseline demographics are illustrated in Table 1. The HIV-infected and control cohorts were matched for age (mean age 38.2 vs. 38.6 years, $p=0.8$). The HIV-infected population included more males (84% vs. 48%, $p<0.0001$) and fewer African-Americans (52% vs. 83%, $p<0.0001$) than the control cohort. In the HIV-infected cohort, mean baseline CD4 count was 219.3 cells/mm³; 48% of subjects had a baseline CD4 count less than 200 cells/mm³. The majority of subjects initiated a non-protease inhibitor (PI)-based therapy (73%).

Baseline mean weight and BMI in HIV-infected persons were lower than in the control cohort (80.0 vs. 92.7 kg, $p<0.0001$; 26.4 vs. 31.9 kg/m², $p<0.0001$, respectively). Baseline BMI categories are illustrated in Fig. 1. At baseline, a smaller proportion of the HIV-infected cohort was overweight/obese (52% vs. 91%, $p<0.001$) compared to the control cohort. Five percent of the obese HIV-infected cohort and 13% of the obese control cohort had a BMI ≥ 40.0 kg/m² at baseline.

Weight and BMI increased significantly during 12 months of initial cART in the HIV-infected group (80.0 to 84.4 kg, $p<0.0001$; 26.4 to 27.9 kg/m², $p<0.0001$, respectively). There were no significant changes in weight or BMI in the control group (92.7 to 93.0 kg, $p=0.5$; 31.9 to 32.0 kg/m², $p=0.6$, respectively). Among HIV-infected persons, there was no significant difference in weight gain as a function of pretreatment weight classification (5.5 kg for underweight or normal vs. 3.5 kg for overweight or obese, $p=0.3$). Among the 44 HIV-infected subjects who were not classified as overweight/obese prior to treatment, 15 became overweight/obese during the first year of cART, 40% of whom became obese. Overweight/obesity prevalence during the first 12 months of cART increased from 52% to 66%, a 27% relative increase ($p=0.002$) (Fig. 1). Overweight/obesity prevalence remained unchanged over 12 months in the control cohort (91% to 92%, $p>0.9$).

Gender-stratified analyses showed a significant increase over 12 months in the prevalence of overweight/obesity in the HIV-infected cohort for males (51% to 64%, $p=0.01$) and a clinically significant increase for females (60% to 80%, $p=0.3$). There were no significant increases in the prevalence of overweight/obesity in the control cohort for males (93% to 93%, $p>0.9$) or females (90% to 90%, $p>0.9$). Race-stratified analyses showed a significant increase over 12 months in the prevalence of overweight/obesity in the HIV-infected cohort for African-Americans (58% to 75%, $p=0.01$) and a clinically significant increase for non-African-Americans (46% to 57%, $p=0.1$). There were no significant increases in the prevalence of overweight/obesity in the control cohort for African-Americans (94% to 94%, $p>0.9$) and non-African-Americans (81% to 81%, $p>0.9$).

FIG. 1. (A) Body mass index (BMI) categories at baseline prior to treatment and 12 months after initial combination antiretroviral therapy in the HIV-infected cohort. (B) BMI categories at baseline and after 12 months of follow-up in the control cohort. BMI categories (kg/m²): underweight (UW) <18.5 , normal 18.50–24.99, overweight (OW) 25.00–29.99, obese (OB) ≥ 30.00 , overweight/obese (OW/OB) ≥ 25.00 .

Changes in weight differed based on subject and treatment characteristics. Weight changes during cART are stratified by categories for the HIV-infected cohort in Table 2. Weight increased significantly for all subcategories, except for persons with baseline CD4 ≥ 200 cells/mm³ and baseline HIV RNA viral load $<100,000$ copies/ml. Differences in weight gain were demonstrated between groups in categories, including gender, pretreatment CD4 count, and cART regimen. Weight gain was greater in HIV-infected females than in males (8.6 vs. 3.6 kg, $p=0.04$). Pretreatment weight was similar for persons initiating PI-based cART compared to non-PI-based cART (81.3 vs. 79.5 kg, $p=0.7$), but weight gain was greater during the use of PI-based cART compared to non-PI-based cART (9.0 vs. 2.7 kg, $p=0.001$). The PI-based cART cohort had a clinically significant greater proportion of persons with a baseline CD4 count <200 cells/mm³ compared to the non-PI-based cART cohort (64% vs. 42%, $p=0.06$). In addition, a

TABLE 2. WEIGHT PRIOR TO TREATMENT AND AFTER 12 MONTHS OF INITIAL COMBINATION ANTIRETROVIRAL THERAPY IN HIV-INFECTED PERSONS

Category	Subcategory	n	Pretreatment (kg)	12 months (kg)	Difference in change within subcategory (kg)	p-value	Difference in change between subcategories (kg)	p-value
Gender	Female	15	83.9±33.1	92.5±30.4	8.6±10.2	0.006	5.0±8.4	0.04
	Male	77	79.2±15.6	82.8±17.1	3.6±8.1	0.0002		
Race/ethnicity	AA	48	83.1±23.0	88.7±22.6	5.6±8.8	<0.0001	2.4±8.6	0.2
	Non-AA	44	76.6±13.8	79.8±15.7	3.2±8.3	0.02		
Age	<40 years	58	78.8±19.4	84.1±21.2	5.3±9.6	0.0001	2.3±8.6	0.2
	≥40 years	34	82.0±19.4	85.0±18.1	3.0±6.3	0.01		
Insurance	Non-Medicaid	82	80.4±19.2	84.3±20.2	4.0±8.4	<0.0001	4.3±8.5	0.1
	Medicaid	10	76.9±21.7	85.1±18.8	8.2±9.6	0.02		
Year of cART initiation	1998–2004	48	77.2±20.7	80.6±20.2	3.4±6.8	0.001	2.2±8.6	0.2
	2005–2008	44	83.0±17.5	88.6±19.2	5.6±10.2	0.0007		
cART	PI-based	25	81.3±22.3	90.3±23.8	9.0±8.3	<0.0001	6.3±8.2	0.001
	Non-PI-based	67	79.5±18.3	82.2±18.1	2.7±8.1	0.008		
Baseline CD4 count (cells/mm ³)	<200	44	75.5±14.7	84.4±17.5	8.9±9.6	<0.0001	8.6±7.5	<0.0001
	≥200	48	84.1±22.1 ^a	84.4±22.3	0.3±4.7	0.7		
Baseline HIV RNA viral load (copies/ml)	<100,000	43	81.4±20.9	84.2±22.3	2.8±9.9	0.07	3.0±8.5	0.1
	≥100,000	49	78.7±18.0	84.5±18.0	5.8±7.1	<0.0001		

^aComparison of pretreatment weight between CD4 count <200 cells/mm³ and ≥200 cells/mm³ subcategory for HIV-infected cohort, $p=0.03$.

Data presented as mean±standard deviation.

AA, African-American; cART, combination antiretroviral therapy; PI, protease inhibitor.

greater proportion of persons initiating PI-based cART had a baseline HIV viral load >100,000 copies/ml compared to persons on non-PI-based cART (80% vs. 43%, $p=0.002$). Persons with a pretreatment CD4 count <200 cells/mm³ weighed less at baseline than persons with a CD4 count of ≥200 cells/mm³ before treatment (75.5 vs. 84.1 kg, $p=0.03$) and demonstrated greater increases in weight than persons with a pretreatment CD4 count of ≥200 cells/mm³ (8.9 vs. 0.3 kg, $p<0.0001$). At 12 months the weight was similar between persons with baseline CD4 counts <200 cells/mm³ and ≥200 cells/mm³ (84.4 vs. 84.4 kg, $p=0.9$).

Among HIV-infected persons classified as overweight/obese after 12 months of initial cART, there was a significant increase in the proportion of persons with hypertension and/or dyslipidemia compared to the pretreatment visit (49% vs. 74%, $p=0.0003$). There was no significant change in the proportion of persons with hypertension and/or dyslipidemia compared to the pretreatment visit among HIV-infected persons classified as underweight or normal after 12 months of initial cART (26% vs. 35%, $p=0.2$). There were no new cases of glucose abnormalities, CVD, or CVA after 12 months of cART for the HIV-infected population.

Although a slight majority (52%) of HIV-infected persons were overweight/obese prior to treatment, weight gain during the first 12 months of cART resulted in a 27% relative increase in the prevalence of overweight/obesity. Greater weight gain occurred in females, persons with lower baseline CD4 counts, and those treated with PI-based cART. The HIV-infected cohort had greater increases in the prevalence of overweight/obesity compared to an age-matched community cohort. Additionally, a greater proportion of overweight/

obese persons had hypertension and/or dyslipidemia after 12 months of cART compared to underweight or normal weight persons. Weight gain and an associated increase in CV risk factors during initial cART constitute a potential mechanism for increased CVD in HIV-infected populations.

The high prevalence of overweight/obese persons in our cohort supports previous data that suggest an emerging obesity epidemic among HIV-infected persons, although longitudinal data and the effect of cART are not well characterized.^{1,2} One of the few longitudinal studies evaluating weight gain occurred in an HIV-infected Navy cohort with several limitations: lack of females, varying duration of follow-up, and inconsistent cART use.² It found that the prevalence of overweight or obese HIV-infected men in two Navy clinics increased over 10 years from 54% at the time of diagnosis to 63%. The present study provides new longitudinal data demonstrating significant increases in the proportion of overweight/obese HIV-infected persons that were evident after only 12 months of initial cART, as compared to a mean 10-year follow-up in the Navy cohort. In fact, the overall proportion of overweight/obese persons among our HIV-infected population after initial cART (66%) was comparable to that of adults in the general U.S. population (68.3%).⁸

The greater increases in weight gain among HIV-infected females compared to males in our cohort support previous suggestions that females are at an increased risk for overweight/obesity.^{1,9} In addition, HIV-infected females may have rates of overweight/obesity comparable to or higher than HIV-uninfected females.^{1,8,10} A greater proportion of HIV-infected females in our cohort was overweight/obese (80% vs. 64.1%) and obese (53% vs. 35.5%) after initial cART

compared to females in the general U.S. population.⁸ Obesity was 2.6 times more common in HIV-infected females compared to an HIV-uninfected control population in one cross-sectional study.¹

Weight increases were greater among persons with lower pretreatment CD4 counts, as has been reported in a study of changes in lean body mass with cART use.¹¹ After 12 months of cART in the present cohort, weight and BMI measurements did not differ by pretreatment CD4 count in contrast to previous reports linking lower pretreatment CD4 counts to higher BMI after cART.² Similar weight in our cohort at 12 months between the baseline CD4 count categories (<200 cells/mm³ vs. ≥200 cells/mm³) may indicate an immune reconstitution scenario with a return to normal health after effective cART in the <200 cells/mm³, although it is unknown whether any significant amount of weight loss occurred prior to initial cART given that we do not know weight trajectories prior to the first visit in the clinic and both cohorts had a mean baseline BMI in the overweight category. The effect of pretreatment CD4 counts and baseline BMI classification on weight gain with cART needs further elucidation in future studies.

PI-based cART was associated with a significantly greater weight gain than was non-PI-based cART, a finding not consistently seen in other studies.^{1,9} Confounding factors contributing to the use of PI-based therapy may have driven the increased weight gain in this cohort, such as illness at initiation of cART as noted by lower CD4 counts and higher HIV viral loads; however, larger longitudinal studies are needed to further elucidate the role these variables play in the difference in weight changes based on type of cART initiated.

The disproportionate number of overweight/obese persons with hypertension and/or dyslipidemia after the first 12 months of cART in our cohort is concerning in a population at increased risk for CVD. Levels of C-reactive protein (CRP), a marker of systemic inflammation, are strongly correlated with adipose tissue mass and the risk of CVD.^{12,13} CRP levels do not decline to levels comparable to an HIV-uninfected cohort following cART use, suggesting that ongoing inflammation is an important mediator.¹⁴ The link between obesity, inflammation, and CVD is a subject of ongoing interest.

There are limitations to our study worth noting. The study population was relatively small because it included only subjects on stable initial cART, excluding many with other medical conditions or on medications that could confound any weight changes. The sample size precluded multivariate analyses or full analyses of stratified data, including combined gender/race, additional races, and a larger number of age categories. Matching was limited to age due to the fact that many screened age-matched control subjects did not return for care within the 12-month study period limiting the pool of potential control subjects. The frequency of newly diagnosed dyslipidemia or glucose abnormalities may be underestimated since these measurements were not available for all subjects. Finally, the duration of length of this study does not allow assessment of the long-term effects of obesity in this relatively young population.

High rates of overweight/obesity in HIV-infected persons after initial cART are alarming, as the cohort mirrors the obesity epidemic prevalent in the general U.S. population whereas prior to cART, wasting typically distinguished HIV-

infected persons from the general population. Larger prospective studies are required to further define risk factors for weight gain and obesity associated with cART. Early prevention may help avoid the detrimental consequences of obesity. Clinical management of HIV-infected persons needs to anticipate weight gain when planning treatment strategies.

Acknowledgments

This publication was made possible with help from the Duke University Center for AIDS Research (CFAR), an NIH funded program (5P30 AI064518), and support from a KL2 awarded to Dr. Lakey through Duke University and the NIH (KL2 RR024127-03). The authors would like to thank Jessica Hogan and Tammy Chin for their assistance with data collection for this project. Portions of the data from this study were presented at the 6th International AIDS Conference on HIV Pathogenesis, Treatment, and Prevention. Rome, Italy, July 17–20, 2011.

Author Disclosure Statement

Dr. Lakey has grant funding from Janssen and Amarin. Dr. Hicks has grant funding from Argos, Bristol-Myers Squibb, Gilead, Janssen, Merck, and ViiV. He serves on the scientific advisory board for Bristol-Myers Squibb, Gilead, Janssen, Koronis, Merck, and ViiV. Dr. Yancy's spouse is a contractor for GlaxoSmithKline and ViiV.

References

1. Amorosa V, Synnestvedt M, Gross R, Freidman H, MacGregor RR, Gudonis D, Frank I, and Tebas P: A tale of 2 epidemics: The intersection between obesity and HIV infection in Philadelphia. *J Acquir Immune Defic Syndr* 2005;39:557–561.
2. Crum-Cianflone N, Tejedor R, Medina S, Barahona I, and Ganesan A: Obesity among patients with HIV: The latest epidemic. *AIDS Patient Care STDs* 2008;22:925–930.
3. NHLBI Obesity Education Initiative: Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: The evidence report. NIH publication no. 98-4083. 1998; U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute, Bethesda, MD.
4. Klein D, Hurley LB, Quesenberry CP, and Sidney S: Do protease inhibitors increase the risk of coronary heart disease in patients with HIV-1 infection? *J Acquir Immune Defic Syndr* 2002;30:471–477.
5. Currier JS, Taylor A, Boyd F, Dezil CM, Kawabata H, Burtcel B, Maa JF, and Hodder S: Coronary heart disease in HIV-infected individuals. *J Acquir Immune Defic Syndr* 2003;33:506–512.
6. Friis-Moller N, Sabin CA, Weber R, D'Arminio Monforte A, El-Sadr WM, Reiss P, Thiebaut R, Morfeldt L, DeWit S, Pradier C, Calvo G, Law MG, Kirk O, Phillips AN, and Lundgren JD: Combination antiretroviral therapy and the risk of myocardial infarction. *N Engl J Med* 2003;349:1993–2003.
7. Law MG, Friis-Moller N, El-Sadr WM, Weber R, Reiss P, D'Arminio Monforte A, Thiebaut R, Morfeldt L, DeWit S, Pradier C, Calvo G, Kirk O, Sabin CA, Phillips AN, and Lundgren JD: The use of the Framingham equation to predict myocardial infarctions in HIV-infected patients: Com-

- parison with observed events in the D:A:D study. *HIV Med* 2006;7:218–230.
8. Flegal KM, Carroll M, Ogden CL, and Curtin LR: Prevalence and trends in obesity among US adults, 1999–2008. *JAMA* 2010;303:235–241.
 9. Crum-Cianflone NF, Roediger M, Eberly LE, Headd M, Marconi V, Ganesan A, Weintrob A, Barthel RV, Fraser S, and Agan BK: Increasing rates of obesity among HIV-infected persons during the HIV epidemic. *PLoS One* 2010;5:e10106.
 10. Boodram B, Plankey MW, Cox C, Tien PC, Cohen MH, Anastos K, Karim R, Hyman C, and Hershow RC: Prevalence and correlates of elevated body mass index among HIV-positive and HIV-negative women in the Women's Interagency HIV Study. *AIDS Patient Care STDs* 2009;23:1009–1016.
 11. Shikuma CM, Zackin R, Sattler F, Mildvan D, Nyangweso P, Alston S, Evans S, and Mulligan K: Changes in weight and lean body mass during highly active antiretroviral therapy. *CID* 2009;39:1223–1230.
 12. Greenfield JR, Samaras K, Jenkins AB, Kelly PJ, Spector TD, Gallimore JR, Pepys MB, and Campbell LV: Obesity is an important determinant of baseline serum C-reactive protein concentrations in monozygotic twins, independent of genetic influences. *Circulation* 2004;109:3022–3028.
 13. Danesh J, Wheeler JG, Hirschfield GM, Eda S, Eiriksdottir G, Rumley A, Lowe GD, Pepys MB, and Gudnason V: C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. *N Engl J Med* 2004; 350:1387–1397.
 14. Ross AC, Armentrout R, O'Riordan MA, Storer N, Rizk N, Harrill D, El Bejjani D, and McComsey GA: Endothelial activation markers are linked to HIV status and are independent of antiretroviral therapy and lipodystrophy. *J Acquir Immune Defic Syndr* 2008;49:499–506.

Address correspondence to:
 Wanda Lakey
 Duke University Medical Center
 Box 3633
 Durham, North Carolina 27710
 E-mail: lakey001@mc.duke.edu