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## Drug Use and Other Risk Factors Related to Lower Body Mass Index among HIV-Infected Individuals

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### Abstract

Malnutrition is associated with morbidity and mortality in HIV infected individuals. Little research has been conducted to identify the roles that clinical, illicit drug use and socioeconomic characteristics play in the nutritional status of HIV-infected patients. This cross-sectional analysis included 562 HIV-infected participants enrolled in the Nutrition for Healthy Living study conducted in Boston, MA and Providence, RI. The relationship between body mass index (BMI) and several covariates (type of drug use, demographic, and clinical characteristics) were examined using linear regression.

Overall, drug users had a lower BMI than non-drug users. The BMI of cocaine users was 1.4 kg/m<sup>2</sup> less than that of patients who did not use any drugs, after adjusting for other covariates ( $p=0.02$ ). The BMI of participants who were over the age of 55 years was 2.0 kg/m<sup>2</sup> less than that of patients under the age of 35, and BMI increased by 0.3 kg/m<sup>2</sup> with each 100 cells/mm<sup>3</sup> increase in CD4 count. HAART use, adherence to HAART, energy intake, AIDS status, hepatitis B and hepatitis C co-infections, cigarette smoking and depression were not associated with BMI in the final model.

In conclusion, BMI was lower in drug users than non-drug users, and was lowest in cocaine users. BMI was also directly associated with CD4 count and inversely related to age more than 55 years old. HIV infected cocaine users may be at higher risk of developing malnutrition, suggesting the need for anticipatory nutritional support.

### Keywords

drug users; cocaine users; BMI; HIV; CD4 count

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## 1. INTRODUCTION

Nutritional status is an important predictor of progression to AIDS and survival of HIV-infected patients (Mangili et al., 2006; Melchior et al., 1999; Ott et al., 1995; Suttman et al., 1995; Tang et al., 2002; Tang et al., 2005; van der Sande et al., 2004). Body mass index (BMI) is an important measure of nutritional status in HIV infected patients. In previous studies, higher BMI has been associated with decreased risk of HIV progression and declines in CD4 cell counts (Jones et al., 2003; Shor-Posner et al., 2000; Shuter et al., 2001).

About one quarter of cases of HIV infection in the US are associated with drug use (Centers for Disease Control and Prevention (CDC), 2007). The associations between drug use and nutrition in the context of HIV infection has not been widely investigated particularly in non-injection drug users. The risk of malnutrition in drug users is likely multifactorial and may be due to (or exacerbated by) lower caloric intake, abnormal gastrointestinal function or metabolism, or direct effects of the drug(s) itself. A study conducted among a Hispanic population showed that the HIV-infected drug users were more likely to experience malnutrition and weight loss than HIV infected individuals who were not-drug users (Forrester et al., 2005). However, scant research has been conducted among other HIV-infected populations to identify the role that specific drugs and other related factors might play in weight loss.

The Nutrition for Healthy Living (NFHL) Study is a prospective cohort study that examines the nutritional and metabolic consequences of HIV infection. This cohort offers a unique opportunity to study differences in the socio-demographic characteristics and nutritional status of HIV-infected people by type of drugs used.

## 2. METHODS

Data for this analysis came from the NFHL cohort for which data were collected from 1995 to 2005 (Mwamburi et al., 2005; Tang et al., 2002; Tang et al., 2005; Wanke et al., 2000; Wilson et al., 2002; Woods et al., 2002). Over 800 participants from the greater Boston and Providence area were enrolled during this period. Eligible participants were HIV-infected adults over 18 years of age. Pregnant women, patients with diabetes, thyroid disease, or any malignancies other than Kaposi sarcoma, and those not fluent in English were excluded from the study.

Beginning in July 2000, we began collecting more detailed information on specific types of recreational drugs used among study participants. Therefore, for the purposes of this cross-sectional analysis we used data from the first visits of participants who were seen after July 2000 (n=562) to ensure that collection of drug use data was consistent.

The dependent variable for this analysis was BMI, which was calculated as weight divided by the square of height ( $\text{kg}/\text{m}^2$ ). The determinant of interest was "current drug use" (self-reported use in the last 6 months), which was categorized as: cocaine use (but no heroin use), any heroin use (including cocaine concurrently), use of other drugs such as marijuana, sedatives, and poppers (but not cocaine and heroin), and no current drug use. Participants in the cocaine and heroin groups could also be using other drugs concurrently.

Additional covariates of interest included age (in years); race (non-white vs. white); gender; education (below high school, high school graduate, and more than a high school education); income below the poverty line (defined as a personal annual income of \$10,000 or less, plus allowances of \$6,000 per year for each additional household member); current employment; cigarette smoking (never, past, current); caloric intake (kcal/day) based on a 3 day food record; CD4 count ( $\text{cells}/\text{mm}^3$ ); chronic diarrhea; current use of highly active antiretroviral

therapy (HAART), AIDS status, opportunistic infections, hepatitis B and C co-infection, year of study visit in three categories (recruitment in 2000, 2001, and 2002 -2005), and standardized measures of food insecurity and depression.

The United States Department of Agriculture (USDA) defines food security as “access by all people at all times to enough food for an active, healthy life”. Food insecurity therefore exists whenever the availability of nutritionally adequate and safe foods or the ability to acquire acceptable foods in socially acceptable ways is limited or uncertain. HIV infection can significantly compromise the food security of affected individuals and households, placing the individual at risk of nutritional insufficiency. The food insecurity scale that we used in the NFHL study was a slightly modified version of the validated Radimer/Cornell measures of hunger and food insecurity (Kendall et al. 1995). This scale measures both household and individual food insecurity. The scale consists of 5 items (for example, “I worry whether the food in my household will run out before there is money to buy more”; or “I am often hungry, but I don’t eat because I can’t afford enough food”), each with three response levels (often true, sometimes true, or never true).

For assessing depression, we used a brief screening instrument developed by Burnam et al., which has been validated in the HIV population (Burnam et al., 1988). This 8-item scale was developed to screen for depressive disorders, particularly those with more recent prevalence of depression.

Antiretroviral medications (ART) adherence was measured by asking patients about their adherence with each of the antiretroviral medication they took in the past week. The number of doses of each medication missed in the last 7 days was recorded. The proportion of missed doses for each medication was then converted into a single score ranging from 0% to 100%. Adherence of 95% or more was chosen as a cut off point for having good adherence (Wilson IB, 2001).

### Statistical analysis

Univariate analyses were conducted to check the distribution of each variable and to describe the characteristics of research participants. Differences in characteristics among the different categories of drug use were compared using the Pearson’s  $\chi^2$  test for categorical variables and the ANOVA F-test for continuous variables. The dependent variable (BMI) was normally distributed. Simple linear regression was performed between BMI and each covariate. The linear relationships between BMI and all continuous variables, such as age and CD4+ cell count, were graphically checked. As age was not linearly related with BMI, age was categorized into approximate 10-year age categories based on the age range of the population (<35, >35 to 45, >45 to 55, >55) and entered into the model as dummy variables. CD4+ cell count was linearly related with BMI and so was kept as a continuous variable.

Multivariate Least Squares regression analysis was then performed. Type of drug use was entered into the model as three dummy variables. All covariates associated with BMI at a level of  $p < 0.10$  in the bivariate analyses were selected into the initial multivariate model. Backwards selection was then used to eliminate variables from the model until all remaining covariates were significant at a level of  $p < 0.05$ . Each covariate was also checked for potential confounding with type of drug use. If the effect estimate of type of drug use changed by  $>15\%$  when the covariate was eliminated, the variable was retained in the model to control for confounding.

Outliers and influential points were checked using residuals, Cook’s D, and Dfbetas (Ramsey and Schafer, 2002; Vittinghoff E et al., 2005). All outlier values were validated by

checking for data entry errors. Since the estimates were similar in the models with and without the outliers, they were kept in the dataset in order to reflect the true population.

This study was approved by the Institutional Review Boards of Tufts-New England Medical Center in Boston and Miriam Hospital in Providence.

### 3. RESULTS

The baseline characteristics of the study population are presented in Table 1. Among 562 subjects, nearly half were current drug users. This included use of injection and non-injection drugs. Thirteen percent of the cohort were cocaine only users, and 11% were any heroin users. Twenty five percent used other drugs such as marijuana, poppers, sedatives, and methadone in the last 6 months.

The average age of the study population was 43 years (range 24 to 74 years). Cocaine only users were younger than the other groups. In our study population, cocaine only users and non-drug users were more likely to be African American, while a higher proportion of any heroin users were Hispanic compared to the other groups.

There were higher proportions of female participants in the any heroin and non-drug using groups compared to the other groups. Participants who used heroin tended to have lower levels of education than the other groups. Users of other drugs (e.g. marijuana, sedatives, and poppers) besides cocaine and heroin were more likely to have a college education. Participants who used heroin were significantly more likely to live below the poverty line than members of the other categories of drug use. Similarly, participants using heroin were more likely to be food insecure at both the individual and household level. While approximately 34%-40% of the cocaine users, other drug users and non-drug users were employed, very few of those who used heroin were employed (15%). A large majority of heroin and cocaine users (70-85%) were also cigarette smokers.

Table 2 shows the clinical characteristics of the study population by type of drug use. The BMI of drug users overall was significantly lower than that of non-drug users. Overall, twelve percent of the study population suffered from chronic diarrhea with no significant differences between groups. More participants in the no drug use group and fewer participants in the cocaine only group reported that they had been trying to lose weight in the past six months. There were no differences between groups in report of those trying to gain weight. Energy intake was significantly different between groups, with the group using other drugs having the highest caloric intake and the no drug use group having the lowest caloric intake (overall  $p=0.02$ ).

HIV/HCV coinfection was very high (84%) among the heroin group but considerably lower among the other three groups (24-33%). On the other hand, the cocaine only, other drugs, and non-drug use groups had higher percentages of HIV/HBV co-infection than the heroin group (41%-47% vs. 20%).

A higher proportion of participants in the heroin group were AIDS-defined at baseline. There were also more participants in the heroin group who had one or more opportunistic infections in the previous six months. Overall, the mean CD4+ cell count among the participants was 446 cells/mm<sup>3</sup> and the median viral load (copies/ml) in this cohort was 2.3 logs. There were no statistical differences across the drug use groups in terms of CD4+ cell count or viral load. Approximately 70% of the cohort overall had been prescribed HAART. Those who reported using cocaine or heroin were significantly less likely to be prescribed HAART than the other two groups. Adherence to ART was also significantly lower among participants using either cocaine or heroin compared to those using other or no drugs.

In the unadjusted models (Table 3), BMI was significantly lower among the cocaine only users and the other drug users compared to the non-drug using group ( $p < 0.001$  for both groups). Other variables significantly associated with lower BMI included age greater than 55 years, trying to gain weight, having an AIDS diagnosis, and having Hepatitis B infection. Being non-white, female, living below the poverty line, having higher CD4+ cell counts, trying to lose weight, having study visits between 2002-2005, and being depressed were all significantly associated with higher BMI. Neither being prescribed HAART, adherence to HAART, energy intake, Hepatitis C infection, general health status, diarrhea, or cigarette smoking were associated with BMI.

In the final multivariate model, the BMI of those who used cocaine was, on average, 1.4 kg/m<sup>2</sup> less than that of those who did not use any drugs, after adjusting for other covariates (Table 3). The BMI of those using any heroin or other drugs did not differ significantly from the BMI of non-drug users. Participants over the age of 55 years had lower BMI than those 35 years of age or younger. Being non-white, living below the poverty line, and trying to lose weight were all significantly and independently associated with higher BMI. BMI was also significantly associated with CD4+ cell counts, with a 0.3 kg/m<sup>2</sup> increase in BMI per 100 cells/mm<sup>3</sup> increase in CD4+ cell count. Trying to gain weight was significantly and independently associated with lower BMI. Being female, energy intake, having AIDS, having hepatitis B, having a study visit between 2002 and 2005, and being depressed all dropped out of the final multivariate model.

#### 4. DISCUSSION

We found that HIV-infected participants who predominantly use cocaine had significantly lower BMI than HIV infected participants who did not use drugs. This association between cocaine use and BMI remained strong even after adjusting for other covariates including age, race, gender, poverty, CD4+ cell count, and individual efforts to gain or lose weight. This analysis also revealed that dietary intake and socioeconomic characteristics do not fully explain the association between cocaine use and compromised nutritional status, as defined by BMI. Other factors such as changes in metabolism may contribute to lower BMI among cocaine (and not heroin) users, however, our study was not designed to examine this.

To our knowledge only one previous paper has examined the relationship between type of illicit drug use and BMI (health status). This is a paper by Forrester et al., 2005 which showed that among Hispanics, HIV positive drug users had a BMI that was significantly lower than that of HIV positive non-drug users. In addition, in the men, cocaine use alone or mixed with opiates was associated with lower BMI (Forrester et al., 2005). Our study found that cocaine use only (not mixed with heroin) was associated with lower BMI, in both men and women of mixed race/ethnicity. Hepatitis infection and energy intake were not independently associated with BMI among participants in either study.

In our study, there was not a statistically significant association between BMI and heroin use. As the sample size of heroin only users was small in this study, heroin users and people who used both heroin and cocaine were collapsed into one group as they were demographically similar. Both groups tended to be female, Hispanic, poor, unemployed, and less educated. A high proportion of them were co-infected with HCV. They were less likely to be prescribed HAART compared to the other groups of drug users, even though their CD4+ cell counts were slightly lower than the other groups. This would imply that heroin users, including those using both heroin and cocaine concurrently, have the most limited access to health care services, tended to delay their engagement with the health care system, and/or tended to postpone initiation of HAART.

The participants in the “other drugs” group, which included users of marijuana, sedatives, and/or poppers (but no cocaine or heroin) had a lower BMI than the non-drug users, but this did not reach statistical significance after adjusting for other covariates. As this group was using various types of drugs concurrently, it is difficult to tease out the effects of any particular drug in this group and its association with BMI from our data.

Age greater than 55 years old was a significant independent determinant of lower BMI compared to patients 35 years of age or younger. This finding seems to contradict that found in the general population in which BMI generally increases with age (Lewis et al., 2000). This finding could be explained by the trend of weight loss among HIV-infected patients regardless of whether or not they were prescribed HAART (Karmon et al., 2005), assuming that older participants have had a longer duration of HIV infection. It is also consistent with other findings that HIV infected patients continue to face risk of weight loss in the era of HAART (Batterham et al., 2002; Tang et al., 2002; Wanke et al., 2000). Although the cocaine group was younger than the other drug use groups and those not using drugs, BMI was still significantly lower in this group, suggesting that the use of this particular drug may directly affect the metabolism or food intake patterns of active users. Although CD4+ cell count is an important influence on BMI in this and previous studies (Batterham et al., 2002; Jones et al., 2003; Maas et al., 1998; Shor-Posner et al., 2000; Zachariah et al., 2006), our data show that CD4 cell counts were similar among the different drug use groups and did not explain the lower BMI among the cocaine users.

The findings of this study should be interpreted with some limitations in mind: the reliability of self-report of drug use is difficult to substantiate, and much of these data were based on self-reported recall. As drug users normally use many different drugs concurrently, it is very difficult to tease out the particular causal mechanism associated with a particular type of drug. The frequency of drug use was not included in this analysis, so we were not able to distinguish the effects of heavier drug use vs. lighter drug use on BMI. Furthermore, the specific effects of heroin on BMI could be not assessed in this study since the group of heroin only users were combined with the group of drug users who used both heroin and cocaine. However, this was the best option for analysis of this data given the small number of heroin users and the similarities of the two groups, as described above. The strengths of this study are that it is the first study, to our knowledge, to examine differences in demographic and clinical characteristics between drug users using different types of drugs. Also, we had a large enough group of predominantly cocaine users to examine the effect of cocaine on BMI. In addition, our study had adequate numbers of female participants and participants of color.

In conclusion, the findings show that BMI is lower among drug users than non-drug users; and that cocaine use (and not heroin) is associated with the lowest BMI among HIV infected patients, even after adjusting for age, race, gender, poverty, CD4+ cell count, and individual efforts to gain or lose weight. Further research should be done in order to explore the changes in metabolism of HIV-infected persons in the setting of cocaine use. The lower BMI of cocaine users could lead to poorer health outcomes compared to other groups.

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Table 1

Demographic characteristics of Nutrition for Healthy Living (NFHL) Study participants (2000–2005) by types of drugs used<sup>1</sup>

Variables	Cocaine only (n=74)	Any Heroin (n=60)	Other drugs (n=139)	No drug use (n=289)	P-value
Age (years – Mean±SD)	41.1 (±7.0)	42.7 (±5.3)	43.9 (±6.7)	43.9 (±8.1)	0.02
Race (N, %)					
Black	34 (46)	13 (22)	28 (20)	119 (41)	<0.001
Hispanic	4 (5)	11 (18)	9 (7)	30 (10)	
White	34 (46)	33 (55)	91 (66)	129 (45)	
Other	2 (3)	3 (5)	11 (8)	11 (4)	
Female (N, %)	14 (19)	22 (37)	36 (26)	108 (37)	0.006
Education (N, %)					
Below high school	12 (16)	19 (32)	19 (14)	66 (23)	<0.001
High school	48 (65)	35 (58)	64 (46)	148 (51)	
College	14 (19)	6 (10)	56 (40)	75 (26)	
Below poverty line (N, %)	38 (57)	50 (85)	56 (42)	144 (52)	<0.001
Individual food insecurity (N%)	32 (43)	35 (58)	41 (30)	83(29)	<0.001
Household food insecurity (N, %)	38 (51)	40 (67)	47 (34)	114 (40)	<0.001
Currently employed (N, %)	26 (35)	9 (15)	55 (40)	99 (34)	0.009
Cigarette smoking (N, %)					
Never smoker	12 (16)	3 (5)	35 (25)	95 (33)	<0.001
Past smoker	10 (14)	6 (10)	32 (23)	71 (25)	
Current smoker	52 (70)	51 (85)	72 (52)	123 (43)	

<sup>1</sup>Based on self-reported drug use in the last 6 months, which was categorized as: "Cocaine only"; no heroin use, but may be using other drugs concurrently; "Any Heroin"; heroin use with or without the concurrent use of cocaine or other drugs; "Other drugs: use of other drugs (e.g. marijuana, sedatives, poppers, etc.) excluding cocaine and heroin; and "No drug use: those currently not using any drugs.

**Table 2**  
Clinical characteristics of Nutrition for Healthy Living (NFHL) study participants (2000–20005) by types of drugs used<sup>1</sup>.

Variables	Mean ± SD or N(%)			P-value
	Cocaine only (n=74)	Any Heroin (n=60)	Other drugs (n=139)	
BMI (kg/m <sup>2</sup> )	25.0±4.1	25.9±4.5	25.3±5.5	27.4±6.0 <0.001
Chronic diarrhea	11 (15)	10 (17)	17 (12)	31 (11) 0.58
Trying to lose weight	11 (15)	11(18)	31 (22)	88 (31) 0.0013
Trying to gain weight	29 (39)	23(38)	49 (35)	79 (27) 0.10
Energy intake (Kcals)	2640 ±1037	2530±1171	2826±1140	2486±991 0.02
Hepatitis B <sup>2</sup>	25 (41)	10(20)	56 (47)	94 (42) 0.008
Hepatitis C <sup>2</sup>	18 (30)	43(84)	28 (24)	75 (33) <.001
AIDS-defined	36(49)	38(63)	66(47)	126(44) 0.05
1 Opportunistic infection	14(19)	18(30)	21(15)	49(17) 0.08
CD4+ (cells per mm <sup>3</sup> )	488 ±352	403 ±272	440 ±270	446 ±285 0.41
Viral load (log <sub>10</sub> copies/ml) (Median (q1, q3))	3.1 (2.3, 4.1)	3.1 (2.3, 3.7)	2.3 (2.3, 3.9)	2.3 (2.3, 3.6) 0.17
HAART use	46 (62)	33 (55)	106 (76)	212 (73) 0.004
Adherence				
Not using ART	24 (33)	23 (39)	23 (17)	56 (19) <0.001
Not adherent	25 (34)	15(25)	35 (25)	81 (28)
Adherent	24 (33)	21(36)	80 (58)	151 (52)
Depressed	28 (38)	30(52)	50 (36)	94 (33) 0.06

<sup>1</sup> Based on self-reported drug use in the last 6 months, which was categorized as: "Cocaine only": no heroin use, but may be using other drugs concurrently; "Any Heroin": heroin use with or without the concurrent use of cocaine or other drugs; "Other drugs: use of other drugs (e.g. marijuana, sedatives, poppers, etc.) excluding cocaine and heroin; and "No drug use: those currently not using any drugs.

<sup>2</sup> Hepatitis B and C: data available for 454 participants (n=61 in Cocaine only group; n=51 in Any heroin group; n=118 in Other drugs group; and n=224 in No drug use group)

**Table 3** Regression analysis of drug use and other covariates on BMI (dependent variable) among participants in the Nutrition for Healthy Living (NFHL) study, 2000-2005.

Characteristics	Unadjusted models			Final multivariate model		
	Coefficient <sup>†</sup>	95% CI	p-value	Coefficient <sup>†</sup>	95% CI	p-value
Drug use type						
No drug use	Ref	---	---	Ref	---	---
Cocaine only	-2.4	-3.8 -1.0	0.001	-1.4	-2.7 -0.2	0.02
Any Heroin	-1.4	-3.0 0.1	0.07	-0.5	-1.9 0.8	0.44
Other drugs	-2.0	-3.1 -0.9	<0.001	-0.9	-1.8 0.1	0.08
Age (in years)						
<=35	Ref	---	---	Ref	---	---
>35 to 45	-0.6	-2.0 0.9	0.46	-0.4	-1.7 0.9	0.58
>45 to 55	-0.1	-1.6 1.5	0.92	-0.2	-1.6 1.1	0.73
>55	-3.4	-5.6 -1.2	0.003	-2.0	-4.0 0.01	0.05
Non-white	1.9	0.9 2.8	<0.001	1.3	0.5 2.2	0.003
Female	2.6	1.6 3.6	<0.001	0.7	-0.2 1.6	0.14
Living below poverty line	1.1	0.2 2.1	0.02	1.1	0.2 1.9	0.02
CD4+ cell count (per 100cells/m <sup>3</sup> )	0.4	0.2 0.5	<0.001	0.3	0.2 0.4	<0.001
Trying to lose weight	5.8	4.8 6.7	<0.001	3.4	2.4 4.4	<0.001
Trying to gain weight	-4.8	-5.8 -3.9	<0.001	-3.3	-4.2 -2.3	<0.001
HAART use	-0.8	-1.8 0.2	0.13			
Adherence						
Not using ART	Ref	---	---			
Not adherence	-1.2	-2.5 0.1	0.08			
Adherence	-0.7	-1.8 0.5	0.27			
Energy intake (per 100 kcals)	-0.04	-0.09 0.002	0.06			
AIDS	-1.4	-2.4 -0.5	0.002			
Hepatitis B <sup>2</sup>	-1.2	-2.2 -0.2	0.015			
Hepatitis C <sup>2</sup>	0.5	-0.5 1.5	0.31			
Calendar year of study visit						

Characteristics	Unadjusted models			Final multivariate model		
	Coefficient <sup>1</sup>	95% CI	p-value	Coefficient <sup>1</sup>	95% CI	p-value
2000	Ref	---	---			
2001	0.8	-0.3 1.8	0.16			
2002–2005	1.2	0.01 2.4	0.05			
Diarrhea (yes vs. no)	-0.13	-1.5 1.3	0.85			
Depression (yes vs. no)	1.1	0.2 2.1	0.02			
Employment (yes vs. no)	-0.5	-1.5 0.5	0.29			
Cigarette smoking						
Never smoker	Ref	---	---			
Past smoker	-0.1	-1.4 1.3	0.91			
Current smoker	-0.8	-2.0 0.3	0.14			

<sup>1</sup> Unstandardized estimate

<sup>2</sup> Missing indicator method used for Hepatitis B when entered into multivariate models