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Lack of Energy: An Important and Distinct Component of HIV-Related Fatigue and Daytime Function

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Abstract

Context—Fatigue is a prevalent symptom among adults living with human immunodeficiency virus (HIV). There is increasing evidence that fatigue and energy are related, yet distinct constructs. Although HIV-related fatigue has been well studied, little is known about perceived energy and how it relates to fatigue, individual characteristics, and other symptoms.

Objectives—To describe the experience of perceived energy in adults with HIV and evaluate its relationship to demographic and clinical characteristics as well as symptoms of fatigue, sleep disturbance, anxiety, depression, and daytime function.

Methods—The design was descriptive, comparative, and correlational. The sample of 318 adults with HIV completed a demographic questionnaire, the Memorial Symptom Assessment Scale, and measures of fatigue, sleep disturbance, anxiety, depressive symptoms, and daytime function. Medical records were reviewed for disease and treatment data. Participants who reported a lack of energy were compared with those who did not on demographic, clinical, and symptom variables. Regression models of perceived energy and its interference with daytime function also were evaluated.

Results—Perceived lack of energy was highly prevalent (65%) and more strongly related to interference with daytime function than more general measures of fatigue severity, even when controlling for other characteristics and symptoms. Like other aspects of fatigue, lack of energy was associated with sleep disturbance, anxiety, and depressive symptoms. Lack of energy was more strongly related to morning fatigue than to evening fatigue.

Conclusion—Lack of energy interferes with daytime function and is not just the inverse of fatigue but a distinct perception that differs from fatigue.

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Disclosures
The authors declare no conflicts of interest.

Keywords

Fatigue; HIV; sleep disturbance; anxiety; depression; signs and symptoms

Introduction

The treatment of patients infected with human immunodeficiency virus (HIV) has improved dramatically and is increasingly focused on symptom management and quality of life. As this population is now living longer, patients are experiencing a number of unrelieved symptoms that impact quality of life (1-3). Fatigue is one of the most prevalent complaints among adults living with HIV, and ranges between 37%-88% of samples surveyed in large studies (4-7). A commonly described component of fatigue is a perceived lack of energy or low vitality. Perceived energy, vitality, and fatigue are often assumed to be interchangeable concepts or opposite ends of the same continuum (2). There is increasing evidence, however, that fatigue and energy are related, yet distinct constructs (8, 9). For example, the Lee Fatigue Scale consists of separate fatigue and energy subscales (10), and the Profile of Mood States includes a subscale measuring fatigue-inertia and a subscale for vigor-activity (11). A recent Rasch analysis of Lee's Visual Analogue Scale–Fatigue indicated that fatigue and energy represented different constructs in a sample of women living with HIV (12).

Studies of people living with HIV have identified numerous correlates of fatigue, such as anxiety (13), depressive symptoms (5, 13), post-traumatic stress (14), and sleep disturbance (15, 16). Conflicting findings have been reported on the relationship between fatigue and CD4+ T-cell count (17, 18) and viral load (7, 14, 19-21). Although HIV-related fatigue has been well studied, comparatively little is known about perceived energy and how it relates to fatigue and other clinical characteristics and symptoms.

Therefore, the objectives of this cross-sectional study were to describe perceived energy in adults living with HIV and compare those who reported a lack of energy with those who did not on demographic and clinical characteristics and related symptoms of fatigue, sleep disturbance, anxiety, and depression. The relationships between lack of energy, fatigue severity, and their interference with daytime function also were explored.

Methods

Participants and Settings

The Symptom and Genetic Study was a prospective, longitudinal study designed to identify biomarkers of the symptom experience of adults with HIV and guided by the Theory of Symptom Management (22). This analysis evaluated data from the initial assessment of adults living with HIV in the San Francisco area. The protocol was approved by the Committee on Human Research at the University of California, San Francisco. All participants provided written informed consent prior to enrollment. Eligible participants were English-speaking adults who were at least 18 years of age and diagnosed with HIV at least 30 days prior to enrollment. Individuals were excluded if they currently used illicit drugs (as assessed by self-report and subsequent drug test), worked a night shift (i.e., at least four hours between 12AM-6AM), or reported having a diagnosed sleep disorder, bipolar disorder, schizophrenia, dementia, or pregnancy within the prior three months.

Measures

In addition to completing the demographic and symptom questionnaires, participants were screened for illicit drug use by a urine drug test (RediCup®, Redwood Toxicology Laboratory, Inc., Santa Rosa CA). CD4+ T-cell count and viral load measures were obtained

from the most recent lab report in the medical record. A demographic questionnaire provided information on age, sex, partner status, children, race/ethnicity, educational background, income, and employment status. In addition, information about time since HIV diagnosis, current anti-retroviral (ARV) therapy, and acquired immune deficiency syndrome (AIDS) diagnosis were collected from each participant.

Perceived Lack of Energy—The Memorial Symptom Assessment Scale (MSAS) was used to assess perceived lack of energy and 31 other symptoms (23). It is a reliable and valid self-report measure of symptoms that has been used in a variety of clinical populations (24, 25), including patients with HIV (26). The MSAS evaluates symptom occurrence in the past week using an endorsement of yes/no, and then asks about frequency (i.e., rarely, occasionally, frequently, almost constantly), severity (i.e., slight, moderate, severe, very severe), and distress (i.e., not at all, a little bit, somewhat, quite a bit, very much) using four- or five-point Likert scales. A composite score is computed for each symptom as the average score on the severity, frequency, and distress scales (23). If the respondent does not report the symptom, the composite score is 0. For this analysis, the "lack of energy" item was used to determine the symptom's occurrence (yes/no) and the "lack of energy" composite score was used as an estimate of energy experience, with higher scores indicating lower energy.

Morning and Evening Fatigue Severity—A four-item version of the Lee Fatigue Scale (LFS) was used to assess fatigue severity in the morning and evening (10). These four items were highly correlated with the 13-item fatigue scale in a previous sample (10) ($r = 0.95$ for morning and 0.91 for evening ratings). None of the items in this scale specifically address a lack of energy, making it a fatigue-specific measure. Participants completed the four items within 30 minutes of awakening to measure morning fatigue and within 30 minutes prior to going to sleep to measure evening fatigue for three consecutive days. Morning fatigue scores were calculated as the mean of the four items across the three mornings, and evening fatigue scores were calculated as the mean of the same four items across the three evenings. Mean scores could range from 0 to 10, with higher scores indicating greater fatigue. The LFS has been used to measure fatigue in healthy individuals (10, 27) as well as in patients with cancer (28) and HIV (29) and has established validity and internal consistency. In this sample, the Cronbach alpha coefficient was 0.93 for the morning and 0.88 for the evening ratings.

Interference With Daytime Function—The Fatigue Severity Scale (FSS) assesses the *impact* of perceived energy deficit and fatigue over the past week (30) and is accepted for use as an indicator of daytime function (12, 31). Findings from recent studies in patients with stroke (32) and patients with HIV (12) indicate that a seven-item version of the FSS has better psychometric properties, thus the seven-item version (FSS-7) was used. Each item is rated from 1 (strongly disagree) to 7 (strongly agree), and the seven items are averaged to yield a score from 1 (no functional problems because of fatigue or lack of energy) to 7 (unable to function because of fatigue or lack of energy). The FSS has well-established test-retest reliability and clearly differentiates between patients with chronic disease and healthy adults (30). In this study, the Cronbach alpha for the FSS was 0.93.

Sleep Disturbance—The General Sleep Disturbance Scale (GSDS) was used to assess perceived sleep (16, 33-35). The GSDS comprises 21 items that evaluate various aspects of sleep disturbance (i.e., quality and quantity of sleep, sleep onset latency, sleep maintenance, excessive daytime sleepiness, medication use) in the past week. Each item is rated on a 0 (never) to 7 (every day) numeric rating scale and the 21 items are averaged to yield a total mean score that could range from 0 (no disturbance in the past week) to 7 (extreme disturbance every day in the past week). Scores of ≥3 indicate a clinically significant level

of sleep disturbance three or more days in the past week. The GSDS has well-established validity and reliability in shift workers, pregnant women, and patients with HIV disease (16, 33-35). In this sample, the Cronbach alpha coefficient for the GSDS was 0.83.

Depressive Symptoms—The Center for Epidemiological Studies-Depression Scale (CES-D) was used to assess the frequency of depressive symptoms in the past week (36). The CES-D consists of 20 items that represent major symptoms in the clinical syndrome of depression. Scores can range from 0 to 60, with scores ≥16 indicating the need for clinical evaluation for major depression. The CES-D has well-established concurrent and construct validity (37, 38). In this study, the Cronbach alpha coefficient for the CES-D was 0.88.

Anxiety—The Profile of Moods State (POMS) Tension-Anxiety subscale (11) was used to assess anxiety in the past week. The subscale comprises nine items selected to represent the major symptoms of anxiety. Scores can range from 0 to 36, and a mean of 8.6 has been documented in HIV-infected outpatients (39). The POMS has well-established concurrent and construct validity (11). In this study, the Cronbach alpha coefficient for the POMS subscale was 0.86.

Statistical Analyses

Data were analyzed using Stata® Version 11.0 (StataCorp LP, College Station, TX) and IBM SPSS™ Version 18.0 (IBM North America, New York, NY). Descriptive statistics were used to summarize the demographic and clinical characteristics of the sample and to calculate the prevalence of lack of energy reported on the MSAS. Differences in demographic and clinical characteristics, as well as symptom severity scores, were evaluated using Chi-square, Fisher's Exact, and independent samples *t*-tests. A P-value < 0.05 was considered statistically significant. Square root transformations were sufficient to normalize skewed distributions. Because males and transgendered participants did not differ with respect to their report of energy, age, CD4+ T-cell count, or race/ethnicity, their data were combined for comparison with females.

Hierarchical linear regression analysis was used to determine the unique contributions of demographic, clinical, and symptom characteristics to the perceived lack of energy composite score. Demographic predictors were entered into the model first (Step 1), followed by clinical (disease and treatment) characteristics (Step 2), related symptoms (Step 3), and ratings of morning and evening fatigue (Step 4). Gender, age, CD4+ T-cell count, ARV therapy, and body mass index were forced into the model for face validity, and other variables correlated with the lack of energy score (Pearson or Spearman $r \geq 0.20$) were retained for the regression analysis. Interactions between the demographic and clinical variables were assessed and included in the model if $P < 0.10$. Model assumptions and fit were evaluated by examination of standardized Pearson residuals to identify outlying observations. In addition, model fit was assessed by the goodness of fit test.

A second hierarchical linear regression was conducted to determine the unique contribution of perceived lack of energy to the variance in interference with daytime function (FSS-7) scores, when controlling for demographic and clinical factors as well as fatigue severity and other symptom measures. The approach was similar to the regression analysis described above, except the dependent variable was interference with daytime function (FSS-7 score). Measures of fatigue severity (morning and evening LFS scores) were entered in Step 4 and the lack of energy composite score (MSAS) was entered as Step 5.

Results

Sample Characteristics

A convenience sample of 350 adults with HIV was enrolled in this study over a three-year period (April 2005 - December 2007). Two had incomplete perceived energy data, 29 were excluded after screening positive for illicit drugs (i.e., cocaine, amphetamine, ecstasy, methamphetamine, or phencyclidine), and one was excluded after being unable to submit a urine sample for screening. The sample was ethnically diverse and predominantly male, which reflects the local population of adults with HIV. Over half (62%) of the 78 women in the sample were African American. Given the low number of participants self-identifying as being of mixed race/ethnicity, Asian/Pacific Islander, Native American, or of a race/ethnicity other than the options provided in the questionnaire, these groups were combined into a single category of "other" for analysis. Most participants were living with HIV for many years, 79% were currently receiving ARV therapy, 52% had an AIDS diagnosis, and most (75%) were receiving medical disability assistance.

Lack of Energy: Prevalence, Frequency, Severity, and Distress

A total of 206 participants (65%) reported "lack of energy" in the prior week on the MSAS. Of those reporting lack of energy, 46% reported that it occurred *frequently* or *almost constantly*, and 27% reported that it was *severe* or *very severe*. When asked how distressing their lack of energy was in the last week, 36% described it as *quite a bit* or *very much* distressing. For the 206 participants who endorsed lack of energy in the past week, their mean composite score for lack of energy (average of frequency, severity, and distress ratings) was 2.3 ± 0.8 (range 0.9 to 4.0).

Differences in Demographic and Clinical Characteristics by Energy Group

As shown in Table 1, with the exceptions of race/ethnicity and level of education, no demographic differences were found between the 206 in the lower energy group and the 112 in the higher energy group. In post hoc analyses, lack of energy was more commonly reported by White/Caucasians (48%) compared with Black/African Americans (30%) ($P < 0.005$). Post hoc contrasts did not identify the subgroup(s) driving the difference in level of education between the energy groups ($P > 0.05$). With respect to clinical characteristics, the energy groups did not differ in viral load, CD4+ T-cell count, or proportion reporting an AIDS diagnosis. However, participants in the lower energy group had been living with HIV for a longer time than the higher energy group, and were more likely to currently take ARV medications compared to the higher energy group (Table 1).

Differences in Related Symptoms by Energy Group

Differences in related symptom scores between the higher and lower energy groups are summarized in Table 2. Participants in the lower energy group reported more sleep disturbance (GSDS), higher anxiety (POMS), and more depressive symptoms (CES-D) than those in the higher energy group. Of note, when the two fatigue-related items ("I felt that everything I did was an effort" and "I could not get going") and one sleep-related item ("My sleep was restless") were removed from the CES-D total score in post hoc analysis, results were similar (data not shown). Similarly, when the seven daytime dysfunction items were removed from the GSDS score in post hoc analysis, results were similar (data not shown).

Lack of Energy and Relationships with Fatigue Severity and Interference with Daytime Function

As expected, the lower energy group had higher morning and evening fatigue severity ratings (LFS) than the higher energy group (Table 2). The lower energy group also had a

higher mean score for interference with daytime function (FSS-7) than the higher energy group. Similarly, the MSAS lack of energy symptom score (average of frequency, severity, and distress rating) was moderately correlated with LFS ratings of morning ($r = 0.47$) and evening ($r = 0.35$) fatigue severity. Correlating only the MSAS *severity* rating for lack of energy with the LFS severity ratings for morning and evening fatigue yielded similar results ($r = 0.43$ and 0.35, respectively). Interference with daytime function (FSS-7) was more strongly correlated with the lack of energy composite score ($r = 0.67$) than with ratings of either morning ($r = 0.44$) or evening ($r = 0.38$) fatigue severity.

Multiple Regression Analysis of Perceived Energy

Results of the linear regression analysis of perceived energy are presented in Table 3. The demographic variables accounted for 8.8% of the total variance in lack of energy scores. Even when controlling for other relevant factors, adults of Black race perceived more energy (i.e., had lower lack of energy scores) than non-Blacks in our sample. A nearly significant interaction between female sex and Black race suggests that Black women may perceive slightly more energy than other women and Black men.

Clinical characteristics only accounted for an additional 2.5% of the total variance in lack of energy scores. ARV therapy was the only significant clinical predictor of perceived lack of energy after controlling for other factors. Being on ARV therapy was associated with lower perceived energy (i.e., higher lack of energy composite score).

After controlling for demographics and clinical characteristics, other symptoms accounted for nearly a third of the variance in the perceived lack of energy composite scores. Not surprisingly, sleep disturbance was the strongest predictor, even after controlling for the effects of other factors. Depressive symptom score (CES-D) also was predictive of lower perceived energy, but anxiety (POMS) was not uniquely associated with perceived energy scores in the full regression model.

Ratings of fatigue severity accounted for only 1.6% of the variance in lack of energy composite scores when controlling for other relevant factors. Morning fatigue was a significant predictor of perceived energy, but evening fatigue was not uniquely associated with energy scores in the full regression model. The full model was significant ($P < 0.001$) and accounted for 44.9% of the variance in perceived energy scores.

Multiple Regression Analysis of Interference with Daytime Function

Results of the linear regression analysis of interference with daytime function (FSS-7) are presented in Table 4. The demographic variables accounted for only 5.8% of the total variance in daytime function. Female gender was the only significant demographic predictor, with females reporting less interference in daytime function than males or transgender adults. Although Black race was predictive of lack of energy, it was not a significant predictor of interference with daytime function and did not interact with gender in this regression model. The effect of clinical factors was small (2.4%), although higher CD4+ T-cell count was significantly associated with greater interference with daytime function.

Other related symptoms accounted for 32% of the variance in interference scores. Unlike the model fit for perceived lack of energy composite score, the variance in interference with daytime function was influenced by anxiety as well as sleep disturbance and depressive symptoms in the full model. However, it should be noted that sleep disturbance and depressive symptoms were associated with more interference with daytime function, whereas anxiety was associated with less interference after controlling for the effects of other factors. Ratings of morning and evening fatigue severity accounted for little of the

variance (3.1%) in interference with daytime function after controlling for demographic, clinical, and related symptom factors. Morning fatigue, which was strongly associated with interference with daytime function in bivariate analyses, was not uniquely associated with interference with daytime function in the multivariate analysis. Finally, lack of energy accounted for 12.7% of the variance in interference with daytime function, a highly significant predictor even after controlling for demographic and clinical factors, related symptoms, and ratings of fatigue. The full model was significant ($P < 0.001$) and accounted for 56.0% of the variance in interference with daytime function (FSS-7) scores.

Discussion

Findings from this study indicate that perceived lack of energy is an important dimension of HIV-associated symptoms that is strongly associated with interference with daytime function. Lack of energy was reported by a majority (65%) of participants in this sample, and nearly half of those experiencing lack of energy described it as frequent or constant, more than 25% described it as severe or very severe, and more than a third described it as quite a bit or very distressing. These findings suggest that lack of energy is a significant problem for adults living with HIV and is similar to other findings for fatigue in this population (6, 14, 17, 19, 21, 40).

As with fatigue symptom experience, lack of energy was strongly associated with sleep disturbance and depressive symptoms. Anxiety also was related to lack of energy in bivariate analyses, but was unrelated when controlling for the effects of both sleep disturbance and depressive symptoms. When controlling for only one of these related symptoms, anxiety remained a significant predictor of lower perceived energy, suggesting that these findings may be reflective of the strong overlap between these three symptoms rather than the relative unimportance of anxiety.

Several findings from the regression analysis of perceived energy are worth noting. First, demographic and clinical factors accounted for relatively little (11.3% combined) of the variance in perceived energy. Second, sleep disturbance (GSDS), was the strongest predictor of lack of energy score. This finding is consistent with the literature suggesting that fatigue and sleep disturbance are inter-related (16, 41-43), and suggests that this relationship applies to perceived energy as well. The magnitude of this relationship may be underestimated in this cohort, given that individuals at risk for more severe sleep disturbance (e.g., illicit drug use, a diagnosed sleep disorder, nightshift workers, pregnant women) were excluded from this sample. Third, lack of energy was still uniquely associated with depressive symptoms, even after controlling for its strong relationship with sleep disturbance, suggesting that this relationship is not simply the result of depression’s impact on sleep. Fourth, morning and evening fatigue ratings explained little variance (1.6%) in perceived energy after controlling for other relevant factors. This may reflect the overlap between fatigue and other symptoms, but also suggests that fatigue and energy may be related, but distinct constructs.

The regression analysis of interference with daytime function also yielded findings worth noting. First, demographic and clinical variables again accounted for a relatively small proportion of the total variance (8.2%). Second, after controlling for the large influence of sleep disturbance, anxiety and depression, the additional contribution of fatigue-specific measures was small (3.1%). Morning fatigue was strongly associated with interference with daytime function in bivariate analyses, but was not significant when controlling for sleep disturbance, anxiety, depression, and evening fatigue, possibly because of the inter-relatedness of these symptoms. Finally, even after controlling for other symptoms and fatigue-specific measures, lack of energy explained an additional 12.7% of the variance in

interference with daytime function (FSS-7 scores). This finding indicates that energy is an important construct in explaining how patients perceive their daytime function experience.

Until now, most studies have focused on fatigue and some have reported on fatigue while actually using a measure of energy. In order to advance our knowledge of fatigue and how it impacts people's lives, it will be important in future research to be more precise in the use of such concepts. The relationship between the constructs of energy and fatigue should be explored in further research.

A number of study limitations should be noted. First, the generalizability of the findings may be limited to the San Francisco Bay Area, as demographic and clinical characteristics of the sample are representative but known to differ from other urban populations with HIV. However, the relatively comprehensive clinical and supportive care for individuals with HIV in this geographic location might be expected to minimize associations observed between perceived lack of energy and other symptoms, thus underestimating their impact in other populations with HIV. Second, the cross-sectional design precludes the establishment of causal relationships among perceived lack of energy and its correlates. Third, the measure of perceived lack of energy was a single item from the MSAS with three related dimensions that were averaged to yield a composite lack of energy score reflecting the participant's experience during the past week. Future studies should consider using a measure specifically designed to assess perceived energy and should ensure that all measures assess experience across the same periods of time. Fourth, only HIV disease-related (ARV) medications were evaluated in the current study. Future studies also need to evaluate the use of medications that may either cause or relieve symptoms associated with fatigue or low energy, sleep disturbance, anxiety, and depression. Finally, the mechanism(s) of low energy in this cohort may be multifactorial and requires further examination. Given these intriguing findings, additional research is warranted to determine the co-occurrence of multiple symptoms among individuals with HIV, their impact on functional status and quality of life, and how these symptoms interact and change over time in relationship to disease trajectory.

Conclusion

Findings from this study have a number of important clinical implications. First, lack of energy was a highly endorsed symptom, and more systematic assessment of perceived energy is warranted in future studies of adults living with HIV. Although fatigue and low energy are related symptoms, perceived energy may be more relevant to functional status and quality of life. Those who report a lack of energy to their health care providers also need to be assessed for co-occurrence of sleep disturbance as well as anxiety and depression.

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Table 1

Demographic and Clinical Characteristics for the Total Sample and by Perceived Lack of Energy

Characteristic		Lack of Energy?		
	Total *n*=318	**No *n*=112 (35%)**	**Yes *n*=206 (65%)**	**Test and Statistical Significance**
Age (years)				
Mean (SD)	45.1 (8.3)	44.7 (8.3)	45.4 (8.4)	$t(316) = 0.7$; $P = 0.499$
Range	22 – 77	22 – 77	26 – 65	
Sex				$P = 0.416$[a]
Male/ Transgender	75%	72%	77%	
Female	25%	28%	23%	
In a relationship	35%	33%	35%	$P = 0.712$[a]
Have children	36%	42%	33%	$P = 0.112$[a]
Race/Ethnicity				**$\chi^2(3) = 20.9$; $P < 0.001$**
Black/African American	39%	55%	30%	
Hispanic/Latino	10%	9%	11%	
White/Caucasian	41%	28%	48%	
Mixed/Asian/Other	11%	8%	12%	
Education				**$\chi^2(3) = 11.6$; $p = .009$**
Some High School or less	15%	20%	12%	
High School Diploma or equivalent	29%	37%	25%	
Some College	33%	26%	37%	
College Degree or Trade School	23%	17%	26%	
Household Monthly Income				$\chi^2(2) = 5.1$; $P = 0.080$
<$1000	69%	76%	66%	
$1000-$1999	22%	20%	23%	
>$2000	9%	4%	11%	
Employment				$\chi^2(2) = 3.3$; $P = 0.191$
Medical leave/disability	75%	71%	77%	
Employed/Student	16%	16%	16%	
Not Employed	9%	13%	7%	

Characteristic		Lack of Energy?		
	Total *n*=318	**No *n*=112 (35%)**	**Yes *n*=206 (65%)**	**Test and Statistical Significance**
BMI (m/kg^2)				$t(316) = 1.0$; $P = 0.325$
Mean (SD)	27.0 (5.5)	27.4 (5.2)	26.8 (5.7)	
Range	14.4 – 59.7	14.4 – 40.0	17.1 – 59.7	
Metabolic Syndrome				
% meeting diagnostic criteria	30%	33%	28%	$P = 0.423$[a]
Time since HIV diagnosis (years)				**$t(316) = 2.5$; $P = 0.015$**
Mean (SD)	12.0 (7.0)	10.8 (6.5)	12.7 (7.1)	
Range	1 – 27	1 –26	1 –27	
AIDS diagnosis	52%	46%	55%	$P = 0.158$[a]
On anti-retroviral (ARV) medication	70%	62%	75%	**$P = 0.014$**[a]
CD4+ T-cell count (cells/mm^3)[b]	*n*=303	*n*=110	*n*=193	
<200, %	17%	15%	19%	$P = 0.348$[a]
Mean (SD)[c]	449 (266)	449 (259)	449 (269)	$t(301) = 0.07$; $P = 0.948$
Range	4 – 1740	4 – 1088	9 – 1740	
Viral load ($\log_{10}$ copies/mL)[b]	*n*=296	*n*=107	*n*=189	
Detectable (≥1.70), %	50%	52%	48%	$P = 0.546$[a]
Mean (SD) of detectable values	3.63 (1.06)	3.63 (1.00)	3.63 (1.09)	$t(145) = 0.01$; $P = 0.994$
Range	1.70 – 5.70	1.88 – 5.70	1.70 – 5.70	

[a] Fisher's Exact Test.

[b] Smaller sample size as a result of missing laboratory values.

[c] Comparisons are based on square-root of CD4+ T-cell count.

Table 2

Related Symptoms, Fatigue Severity, and Interference With Daytime Function for the Total Sample and by Reported Lack of Energy

Symptom Inventory	Total Sample *n*=318[a]	Lack of Energy?		Test and Statistical Significance
		No *n*=112	Yes *n*=206	
Related Symptoms				
Sleep Disturbance (GSDS)				$t(314) = 9.0$; $P < 0.001$
Mean (SD)	2.1 (1.0)	1.5 (0.8)	2.5 (0.9)	
Range	0.1 - 5.5	0.1 - 3.8	0.5 - 5.5	
Anxiety (POMS)				$t(307) = 7.5$; $P < 0.001$
Mean (SD)	8.7 (7.0)	5.4 (5.8)	10.5 (7.0)	
Range	0 – 35	0 - 28	0 - 35	
Depression (CES-D)				$t(314) = 6.9$; $P < 0.001$
Mean (SD)	16.9 (10.4)	12.2 (9.4)	19.4 (10.1)	
Range	0 – 57	0 - 47	1 - 57	
Fatigue Measures				
Morning fatigue severity (LFS)				$t(316) = 7.9$, $P < 0.001$
Mean (SD)	3.6 (2.3)	2.3 (2.1)	4.3 (2.1)	
Range	0 – 10	0 - 10	0 – 9.5	
Evening fatigue severity (LFS)				$t(192^{b}) = 5.1$, $P < 0.001$
Mean (SD)	5.3 (2.2)	4.4 (2.4)	5.7 (1.9)	
Range	0 – 10	0 - 10	0 - 10	
Interference with Daytime Function (FSS-7)				$t(314) = 10.6$, $P < 0.001$
Mean (SD)	3.8 (1.7)	2.6 (1.3)	4.4 (1.5)	
Range	1 – 7	1 - 6	1 - 7	

GSDS = General Sleep Disturbance Scale; POMS = Profile of Mood States (Tension-Anxiety Subscale); CESD = Center for Epidemiological Studies – Depression; LFS = Lee Fatigue Scale; FSS-7 = 7-item version of the Fatigue Severity Scale (a measure of interference with daytime function); SD = standard deviation.

[a] Two participants in the lower energy group did not complete the GSDS, CESD, or FSS-7 (n=316), and five participants in the lower energy group and four in the higher energy group did not complete the POMS (n=309).

[b] Degrees of freedom adjusted for separate variance t-test, n=318 for the comparison of evening fatigue severity.

Table 3

Linear Regression Analysis of MSAS Lack of Energy Composite Score (*N*=293)

Predictor	*R*	β (full model)	*P*-value (full model)	Δ in R^2
Step 1: Demographics				.088
Female	0.015	0.113	0.109	
Black race	-0.260	-0.117	**0.043**	
Female*Black race interaction	-0.146	-0.148	0.058	
Age (years)	0.014	0.039	0.393	
Step 2: Clinical Characteristics				0.025
CD4+ T-cell count	-0.066	-0.074	0.101	
On ARV therapy	0.127	0.097	**0.037**	
BMI (kg/m2)	-0.074	-0.011	0.821	
Step 3: Other Symptoms				0.320
Sleep disturbance (GSDS)	0.574	0.360	**<0.001**	
Depressive symptoms (CES-D)	0.481	0.159	**0.014**	
Anxiety (POMS)	0.418	0.050	0.398	
Step 4: Fatigue				0.016
Morning fatigue (LFS)	0.466	0.138	**0.035**	
Evening fatigue (LFS)	0.346	0.023	0.711	
Full Model: $F(12,280) = 19.0$, $P < 0.001$				0.449

Demographic and clinical characteristics were forced into the model for face validity and did not need to meet the criterion that $r \geq 0.20$ for inclusion in the model.

Table 4

Linear Regression Analysis of Interference With Daytime Function (FSS-7 Scores, *N*=293)

Predictor	*R*	β (full model)	*P*-value (full model)	Δ in R^2
Step 1: Demographics				0.058
Female	-0.073	-0.095	**0.028**	
Black race	-0.240	-0.057	0.221	
Age (years)	0.014	0.030	0.462	
Step 2: Clinical Characteristics				0.024
CD4+ T-cell count	-0.119	-0.098	**0.016**	
On ARV therapy	0.080	-0.023	0.584	
BMI (kg/m2)	-0.081	0.001	0.983	
Step 3: Other Symptoms				0.320
Sleep disturbance (GSDS)	0.558	0.214	**<0.001**	
Depressive symptoms (CES-D)	0.451	0.129	**0.028**	
Anxiety (POMS)	0.325	-0.111	**0.038**	
Step 4: Fatigue				0.031
Morning fatigue (LFS)	0.452	0.012	0.832	
Evening fatigue (LFS)	0.391	0.140	**0.011**	
Step 5: Energy				0.127
Lack of energy score (MSAS)	0.687	0.477	**<0.001**	
Full Model: $F(12,280) = 29.6$, $P<0.001$				0.560

Demographic and clinical characteristics were forced into the model for face validity and did not need to meet the criterion that $r \geq 0.20$ for inclusion in the model.