Sleep Apnea Symptoms as a Predictor of Fatigue in an Urban HIV Clinic

Umesh Goswami, MD,^{1,4} Jason V. Baker, MD, MS,^{2,4} Qi Wang, MS,³
Wajahat Khalil, MD,¹ and Ken M. Kunisaki, MD, MS¹

Abstract

Fatigue is common among persons living with HIV (PLWH), and risk factors for obstructive sleep apnea (OSA) such as older age and obesity are increasingly prevalent. Studies of OSA among PLWH are lacking, so we aimed to characterize OSA symptoms and associated clinical consequences (e.g., fatigue) among a contemporary population of PLWH. Self-administered surveys containing 23 items that included self-reported snoring, witnessed apneas, estimated sleep duration, the Epworth Sleepiness Score (ESS), and the FACIT-Fatigue score were mailed to PLWH receiving care at an urban HIV clinic. Clinical/demographic data were collected from the medical record. Multivariable linear regression models were created to study relationships between fatigue, clinical variables, and OSA symptoms. Of 535 surveys, 203 (38%) responded. Eight patients (3.9%) had known OSA. Among those without known OSA, mean respondent characteristics included: age 47 years; 80% male, 41% African American, 48% Caucasian, BMI 26.4 kg/m², duration of HIV diagnosis 12 years, 93% on antiretroviral therapy, and 81% with <50 HIV RNA copies/mL. 27% reported snoring, 24% reported witnessed apneas, and 38% had excessive daytime sleepiness. Witnessed apnea was the strongest independent predictor of fatigue (lower FACIT-Fatigue score; $\beta = -6.49$; $p < 0.001$); this difference of 6.49 points exceeds the accepted minimal clinically important difference of 3.0 points. Other predictors included opioid use ($\beta = -5.53$; $p < 0.001$), depression ($\beta = -4.18$; $p = 0.02$), antidepressant use ($\beta = -4.25$; $p = 0.02$), and sleep duration <6 h ($\beta = -3.42$; $p = 0.02$). Our data strongly support the need for increased efforts directed at OSA screening and treatment in PLWH.

Introduction

FATIGUE IS ONE OF THE MOST COMMON self-reported and provider-identified symptoms in persons living with HIV/AIDS (PLWH)¹ with a prevalence ranging from 60% in HIV infection^{2,3} to 85% among those with AIDS.³ Several predictors of fatigue are common in this population, including systemic inflammation, anxiety, depression, chronic pain, aging, medical co-morbidities, and sleep disturbances.³⁻⁷ Antiretroviral treatment (ART) medications themselves may induce fatigue, although data from the era prior to effective ART and the modern ART era show a similarly high prevalence of fatigue, and a large cohort study showed no overall relationship between ART use and fatigue.⁸

The sleep disturbances studied to date, and associated with fatigue in PLWH,^{3,9} have included insomnia, poor self-reported sleep quality, and increased sleep fragmentation.¹⁰ Fatigue and excessive daytime sleepiness are the most common symptoms of obstructive sleep apnea (OSA)¹¹ and

despite several reasons to hypothesize that PLWH are at higher risk than the general population for developing OSA, few studies have described the prevalence and/or factors contributing to OSA among PLWH.

OSA is caused by repeated closure of the upper airway during sleep, resulting in frequent arousals and sleep fragmentation. Untreated OSA results in excessive daytime sleepiness, with clinical consequences such as reduced quality of life and an increased risk of motor vehicle accidents.¹² Prospective cohort studies have also demonstrated that the presence of OSA is a risk factor for cardiovascular disease¹³—hypertension, coronary artery disease, heart failure, cardiac arrhythmias, pulmonary hypertension, and stroke; metabolic syndrome¹⁴ with development of insulin resistance and obesity; and neurocognitive dysfunction¹⁵ including memory loss, dementia, and frailty.¹⁶

The traditional OSA risk factors of older age and obesity are becoming more prevalent among PLWH,¹⁷ but several other HIV associated factors also predispose to development

Departments of ¹Pulmonary, Critical Care, Allergy, and Sleep Medicine, ²Infectious Diseases, and ³Biostatistics, University of Minnesota, Minneapolis, Minnesota.

⁴Hennepin County Medical Center, Minneapolis, Minnesota.

of OSA. These relate to increased upper airway infections leading to adenotonsillar hypertrophy,¹⁸ antiretroviral medication-induced cervical fat redistribution,^{19,20} and HIV-associated inflammatory cytokine production,²¹ possibly resulting in impaired neuromuscular control of upper airway patency during sleep. Despite this clustering of biological and epidemiological risks for developing OSA, a recent large ($n=7324$) cohort study reported²² that PLWH are less likely to be tested for and diagnosed with OSA compared to uninfected controls. Therefore, the true prevalence of OSA in PLWH remains unknown and its impact on clinical symptoms and HIV co-morbidities such as cardiovascular, metabolic, and neurocognitive disease are unclear.

In order to address the knowledge gaps in this area, we surveyed PLWH for symptoms of obstructive sleep apnea, and assessed the relationship between such symptoms and the common HIV clinical symptom of fatigue. We hypothesized that obstructive sleep apnea symptoms are frequent in PLWH and are independent predictors of HIV-associated fatigue.

Methods

Study participants and recruitment methodology

All participants in this study were patients currently receiving medical care at the Hennepin County Medical Center (HCMC) HIV clinic ['Positive Care Center' (PCC)] in Minneapolis, Minnesota, USA. The PCC provides primary and specialty healthcare for over 2000 PLWH. Three of the 10 different HIV providers in the clinic participated in the study; their corresponding panel of patients totaled approximately 1200 persons. Study participants were identified via a computer-generated randomly ordered list.

Selected study participants received a two-page mailed survey (see supplementary material at www.liebertpub.com/apc) along with an introductory letter defining the goals of the study. The letter made no reference to HIV infection or HIV status and included a pre-paid and addressed envelope. In order to increase the study participation, a modified version of the Dillman Total Design Method²³ was employed. This involved a second mailing with a reminder cover letter and a copy of the original survey questionnaire to all patients who did not respond within 2 weeks of the initial mailing. Respondents were also given a small (\$5 retail store gift card) monetary compensation. The surveys were mailed in batches of 200 each until the pre-specified recruitment goal of 200 completed surveys was met. The study protocol was approved by the HCMC Human Subjects Research Committee.

Survey content

The self-administered survey contained 23 items, including (1) three questions regarding habitual self-reported snoring, witnessed apneas, and estimated sleep duration; (2) a modified version of the Epworth Sleepiness Score (ESS)²⁴ to quantify excessive daytime sleepiness; and (3) the Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) subscale.²⁵

The ESS describes eight different situations from daily life, and quantifies the likelihood of falling asleep, rated on an ordinal scale of no chance, slight chance, moderate chance, or high chance of falling sleep in each of the described situations. The ESS is the most commonly used

measure of self-reported sleepiness, is scaled from 0 to 24 points, with scores of >10 widely considered to reflect excessive daytime sleepiness as confirmed with objective tests for measuring excessive daytime sleepiness. FACIT-F is a 13-item questionnaire designed to assess the impact of self-reported fatigue and its impact upon daily activity and function. All 13 items are equally weighted and scored on a scale of 0 to 4, yielding a final score between 0 and 52 with lower scores reflecting increasing levels of fatigue; the minimal clinically important difference is widely considered to be 3 points.²⁶

For respondents, we created a sleep apnea risk score based on the STOP-BANG (Snoring, Tiredness, Observed apnea, high blood Pressure, BMI > 35 kg/m², Age > 50 years, Neck circumference > 40 cm, male Gender)²⁷ questionnaire, which is a simple and widely used OSA risk screening tool. Neck circumference could not be assessed via our mailed survey methodology, so we utilized a score that did not include neck circumference (i.e., STOP-BAG). STOP-BAG scores were computed by including relevant questionnaire items and clinical and anthropometric variables obtained from the electronic medical record review. For analyses directed at studying predictors of fatigue, we removed the (T)iredness component, resulting in a composite SOP-BAG score, in order to prevent tiredness from being in both the dependent and independent variables at the same time.

Other co-variables

Baseline clinical variables were obtained from review of the electronic medical record. These included demographic variables, anthropometric measurements, co-morbid disease conditions, prescribed medications (including antiretroviral medications), HIV disease parameters (including time since diagnosis, current and nadir CD4 count, and HIV RNA), and social parameters such as smoking status, alcohol use, illicit drug use, and employment status. All variables were recorded for respondents and a random sample (10%) of the non-respondents for comparison.

Statistical analysis

Two-sample *t* test and Chi-square tests were used to compare survey respondents and non-respondents for continuous and categorical variables, respectively. Spearman correlation coefficients examined the relationship between FACIT-F, SOP-BAG/STOP-BAG, and ESS scores. Multi-variable backwards stepwise linear regression analysis was used to evaluate the association between the dependent variable of FACIT-F score and independent variables, including demographic characteristics, co-morbidities, HIV variables, medications, and OSA symptoms. SAS version 9.3 (SAS Institute Inc., Cary, NC) was used for statistical analysis.

Results

A total of 600 survey questionnaires were mailed, out of which 535 were delivered (64 of the undelivered surveys were due to wrong or changed address and 1 due to the patient being deceased since their most recent HIV clinic visit). Of the delivered surveys, 203 (38%) were completed and returned. Compared to the 203 respondents, the random sample of 30 non-respondents were more likely, based on chart

review, to have documented active recreational drug use (85.7% vs. 43.0%), less likely to have a diagnosis of anxiety disorder (13.3% vs. 33.3%), and less likely to have been prescribed antidepressant medications (20.0% vs. 40.0%). Age, BMI, and HIV disease parameters did not differ between the respondents and non-respondents.

Of respondents, 8 (3.9%) carried a previous diagnosis of OSA. As expected, compared to those without a previous OSA diagnosis, these patients had more STOP-BAG risk factors for OSA, such as BMI >35 kg/m², snoring and witnessed apneas (Table 1). These 8 respondents were excluded from subsequent analyses.

The mean duration of HIV diagnosis for respondents without OSA was 11.9 ± 7.1 years. 81% were on ART with a mean current CD4 cell count of 579 ± 284 cells/mm³. The majority of the patients (81%) had undetectable viral load; 52 (27%) participants reported loud snoring, and 47 (24%) reported witnessed apneas. The mean duration of nightly self-reported sleep was 6.2 ± 1.5 h, and 56% reported ≤6 h of nightly sleep. The mean ESS was 8.7 ± 5.4 with 33.8% reporting ESS >10, indicating excessive daytime sleepiness. The mean FACIT-F score among this group was 32.5 ± 12.6, which is worse than the general population mean of 40.1 ± 10.4. Demographic, HIV, co-morbidity, sleep, and fatigue characteristics of the responders are listed in Table 2.

In correlational analysis, a statistically significant but weak negative correlation was noted between FACIT-F score and the composite sleep apnea risk score (SOP-BAG) ($r = -0.18$, $p = 0.01$) and a weak positive correlation was noted between ESS and SOP-BAG score ($r = 0.17$, $p = 0.02$), suggesting that those with higher OSA risk had more fatigue and more excessive daytime sleepiness. The correlation between FACIT-F score and ESS was moderate ($r = -0.52$, $p < 0.0001$).

In stepwise backward multivariable linear regression (Table 3), witnessed apnea was the strongest independent predictor of increased fatigue ($\beta = -6.49$; $p < 0.001$). This suggests that the presence of witnessed apnea is associated with a FACIT-F score nearly 6.5 points lower than in those without witnessed apnea. Lower FACIT-F scores indicate increasing fatigue and this difference of nearly 6.5 points exceeds the minimal clinically important difference of 3 points for the FACIT-F score.

TABLE 1. STOP-BAG SLEEP APNEA SYMPTOMS AND RISK FACTORS AMONG SURVEY RESPONDENTS WITH AND WITHOUT A PREVIOUS OSA DIAGNOSIS

Variable	Respondents	
	Without OSA (n = 195)	With OSA (n = 8)
Snoring, %	27%	57%
Tiredness, ^a %	93%	87%
Observed apneas, %	24%	71%
High blood Pressure, %	28%	38%
BMI > 35 kg/m ² , %	5%	38%
Age > 50 years, %	37%	25%
Male Gender, %	85%	75%

^aTiredness in this analysis was defined as any positive response to the FACIT-Fatigue question, "I feel tired", including "a little bit," "somewhat," "quite a bit," and "very much."

TABLE 2. CHARACTERISTICS OF RESPONDENTS (N=195) WITHOUT PREVIOUS DIAGNOSIS OF OSA

Age, years	46.5 ± 10.1
>50 years	37%
>65 years	2%
Male gender, %	80%
Race, %	
Caucasian	46%
African American	42%
Hispanic	5%
Other	7%
Employment status, %	
Employed	37%
Unemployed	61%
Unknown	2%
BMI, kg/m ²	26.4 ± 5.7
>25 kg/m ²	57%
>35 kg/m ²	5%
HIV duration, years	11.9 ± 7.1
CD4 count current, cells/mm ³	579 ± 284
CD4 nadir, cells/mm ³	235 ± 158
HIV RNA, <50 copies/mL, %	81
Currently on ART, %	81%
Active smoker, %	63%
Active alcohol use, %	78%
Active IDU, %	43%
Medical co-morbidities, %	
Hypertension	28%
Diabetes mellitus	8%
Coronary artery disease	4%
Stroke	1%
Arrhythmia	2%
Depression	55%
Anxiety	33%
Current medications, %	
Narcotic	37%
Benzodiazepine	11%
Non-benzodiazepine hypnotic	18%
Antidepressant	40%
Self-reported sleep duration, hours	6.2 ± 1.5
Self-reported sleep ≤6 h	56%
Epworth Sleepiness Score (ESS)	8.7 ± 5.4
ESS >10 points, %	34%
Snoring, %	27%
Witnessed apneas, %	24%
FACIT-Fatigue score	32.5 ± 12.6

Data shown as mean ± standard deviation or proportion (%)

ART, antiretroviral treatment; BMI, body mass index; IDU, injection drug use.

Other predictors of increased fatigue included opioid use ($\beta = -5.53$; $p < 0.001$), depression ($\beta = -4.18$; $p = 0.02$), antidepressant use ($\beta = -4.25$; $p = 0.02$), and self-reported sleep duration <6 h ($\beta = -3.42$; $p = 0.02$). Being unemployed was associated with less fatigue ($\beta = 5.66$; $p = 0.0003$). Older age, BMI, and CD4 count were not related to fatigue.

Discussion

These survey data describe the association between self-reported OSA symptoms, fatigue, and excessive daytime sleepiness among PLWH. Within this urban HIV clinic, we found a high prevalence of snoring, witnessed apnea, and fatigue. More importantly, witnessed apnea was the strongest

TABLE 3. FINAL MULTIVARIABLE STEPWISE LINEAR REGRESSION MODEL FOR OUTCOME OF FACIT-FATIGUE QUESTIONNAIRE SCORE AMONG SURVEY RESPONDENTS WITHOUT A PREVIOUS OSA DIAGNOSIS (N=195)

Variable	Regression Coefficient (β)	p Value
Intercept	38.51	<0.0001
Witnessed apnea	-6.49	0.0002
Opioid use	-5.53	0.0005
Antidepressant use	-4.25	0.018
Depression	-4.18	0.019
Sleep duration ≤ 6 h	-3.42	0.023
Unemployed	5.66	0.0003

Regression coefficients (β) represent the difference in FACIT-Fatigue score in presence versus absence of the corresponding factor. Lower FACIT-Fatigue scores indicate increased fatigue. The minimal clinically important difference in FACIT-Fatigue score is 3 points.

independent predictor of fatigue in this population. Our data suggest that OSA (as suggested by the prevalence of its symptoms) may be more common among PLWH than previously thought—a clinically important finding given that OSA is associated with a broad spectrum of health consequences and is a treatable cause of fatigue.

Fatigue is a very common, debilitating, and difficult-to-treat symptom in PLWH.^{28,29} Most studies exploring the predictors of fatigue in PLWH have noted that instead of HIV-related factors such as CD4 count and viral load, self-reported sleep disturbances are the strongest correlates of fatigue.^{3,30} There is a high prevalence of various sleep disorders in PLWH. Up to 70% of PLWH experience difficulty initiating and maintaining sleep,³¹ 47% report poor sleep quality,³² and 20–50% report excessive daytime sleepiness.³³

In addition to these sleep disorders, PLWH are increasingly developing typical risk factors for OSA such as obesity and aging.^{20,22,34,35} Conditions like insomnia, poor night time sleep, and excessive daytime sleepiness may also directly result from the frequent arousals caused by OSA and can have important consequences that influence HIV disease outcomes such as adherence to medications.³⁶

There remains a paucity of studies that have explored the association of OSA with fatigue and other sleep disorders in PLWH. Patil and colleagues³⁴ enrolled 159 men who have sex with men (60 without HIV and 99 with HIV—58 treated with ART treatment and 41 with no ART for at least 1 year) and performed overnight polysomnography. They found a very high prevalence of OSA (70.7% in those with HIV with ART use, 73.2% in those with HIV but no ART use, and 86.7% in those without HIV) among all participants. Fatigue was more commonly reported by those with HIV than those without (25.5% vs. 6.7%), but sleep apnea was not associated with increased fatigue in this sample of PLWH.

We note several important differences between our study and the study by Patil and colleagues³⁴ that may explain the lack of association between fatigue and OSA in their study. Although their study included detailed measurement of sleep parameters in all participants using overnight in-lab polysomnography (the gold standard for diagnosis of OSA), the assessment of fatigue was based only on two questions asking about feeling of tiredness for 3 consecutive days for 2 or more weeks. HIV-associated fatigue is a complex, multidimen-

sional process that has several important facets and attributes.^{37,38} We addressed this by employing the FACIT-Fatigue scale that provides much broader assessment of fatigue symptoms and has been previously validated in PLWH.²⁵ Patil and colleagues also studied only men, while our patient population included 19% women.

Another important difference between our study participants and the cohort described by Patil and colleagues was that the majority (81%) of our patients were currently on ART, compared to only 41% in their study. This may be important since their study found that those who had ever been exposed to ART had much higher prevalence of OSA (90% vs. 57.2%, $p=0.02$) and had higher prevalence of fatigue (31.6% vs 17.1%, $p=0.16$).

The results of our study underscore the potential importance of screening for OSA in PLWH. Data from the Veterans Aging Cohort Study²² showed that despite more frequent self-reported fatigue and daytime somnolence in PLWH compared to those without HIV infection, sleep studies for evaluation of OSA were much less frequently performed in PLWH. The under-recognition of this potentially treatable cause of HIV-associated fatigue and several other important health consequences could relate to the fact that PLWH might have different risk factors for OSA than the general population.

Several studies^{21–23} have reported that PLWH with OSA are usually younger, have lower BMIs, and are less likely to be hypertensive than HIV-uninfected OSA patients, perhaps reducing the sensitivity and specificity of common screening tools for OSA such as the STOP-BANG questionnaire. This may also explain why we did not find a strong correlation between the composite OSA risk score and fatigue score. The pathogenesis of OSA in HIV may also be driven by inflammatory cytokines,^{21,39,40} resulting in impaired neuronal control of upper airway musculature during sleep. In addition, other molecular and genomic attributes of HIV^{41,42} may also explain the occurrence of certain sleep disorders in this population. The lack of basic understanding of OSA pathogenesis in PLWH requires extensive further study to test these hypotheses.

OSA symptoms are highly prevalent in PLWH compared to the general population. In this study, 27% of participants reported snoring and 24% reported witnessed apneas. While the proportion of snorers is comparable to that found in the general population, the proportion reporting witnessed apneas was significantly larger than the 2–4% reporting witnessed apneas in community-dwelling populations⁴³ and the 11–21% among those who have been referred to a sleep clinic for evaluation of OSA.⁴⁴ Witnessed apneas have been shown to be a strong predictor of both mild OSA [odds ratio (OR) of 4.51 [95% confidence interval (CI): 0.8–26.4] in age and sex adjusted models] and moderate to severe OSA [OR 9.74 (95% CI: 1.8–51.7)].^{45,46} Our data therefore suggest that PLWH with fatigue should be asked about witnessed apneas and if present, such patients may benefit from referral for sleep testing.

Our study has several important limitations. In this study, we relied on participants' self-report of OSA and fatigue symptoms without objective sleep studies to confirm the presence or absence of sleep apnea. Although witnessed apneas are a predictor of OSA, the lack of confirmatory sleep testing in our study precludes us from definitively relating

OSA to fatigue in PLWH. Another limitation of our study pertains to the response bias inherent with a survey-based study design. Respondents may have been more fatigued and concerned with sleep disturbances than non-respondents. There were no differences between respondents and non-respondents in regard to OSA risks like age and BMI, nor HIV disease variables. However, respondents had more anxiety and depression and therefore may also over-report fatigue.

In conclusion, PLWH have a high prevalence of fatigue and excessive daytime sleepiness. Witnessed apneas were the strongest predictor of increased fatigue. Our data support the need for heightened efforts to screen, test, and treat for sleep apnea in PLWH.

Acknowledgments

We thank the participants in this study.

Funding support: Biostatistical analysis for this study was provided by the University of Minnesota Clinical and Translational Science Institute Biostatistical Design and Analysis Center, funded by the National Center for Advancing Translational Sciences of the National Institutes of Health, Award Number UL1 TR000114.

Disclaimer: The views expressed in this article are those of the authors and do not reflect the views of any of the authors' affiliated institutions.

Author Disclosure Statement

None of the authors have conflicts of interest to declare.

References

- Justice AC, Rabeneck L, Hays RD, Wu AW, Bozzette SA. Sensitivity, specificity, reliability, and clinical validity of provider-reported symptoms: A comparison with self-reported symptoms. *J Acquir Immune Defic Syndr* 1999;21:126–133.
- Barroso J, Carlson JR, Meynell J. Physiological and psychological markers associated with HIV-related fatigue. *Clin Nurs Res* 2003;12:49–68.
- Phillips KD, Sowell RL, Rojas M, Tavakoli A, Fulk LJ, Hand GA. Physiological and psychological correlates of fatigue in HIV disease. *Biol Res Nurs* 2004;6:59–74.
- Merlin JS, Walcott MM, Herbey I, Chamot E, Ritchie C, Saag MS, Kertesz S. Qualitative investigation of a brief chronic pain screening tool in HIV-infected patients. *AIDS Patient Care STDS* 2014;28:176–182.
- Hasse B, Ledergerber B, Furrer H, et al. and Swiss HIV Cohort Study. Morbidity and aging in HIV-infected persons: The Swiss HIV cohort study. *Clin Infect Dis* 2011;53:1130–1139.
- Kim DJ, Westfall AO, Chamot E, et al. Multimorbidity patterns in HIV-infected patients: The role of obesity in chronic disease clustering. *J Acquir Immune Defic Syndr* 2012;61:600–605.
- Rodriguez-Penney AT, Iudicello JE, Riggs PK, et al. and The HIV Neurobehavioral Research Program HNRP Group. Co-morbidities in persons infected with HIV: Increased burden with older age and negative effects on health-related quality of life. *AIDS Patient Care STDS* 2013;27:5–16.
- Silverberg MJ, Gore ME, French AL, et al. Prevalence of clinical symptoms associated with highly active antiretroviral therapy in the Women's Interagency HIV Study. *Clin Infect Dis* 2004;395:717–724.
- Jong E, Oudhoff LA, Epskamp C, et al. Predictors and treatment strategies of HIV-related fatigue in the combined antiretroviral therapy era. *AIDS* 2010;24:1387–1405.
- Taibi DM. Sleep disturbances in persons living with HIV. *J Assoc Nurses AIDS Care* 2013;24:S72–S85.
- Chervin RD. Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. *Chest* 2000;118:372–379.
- Teran-Santos J, Jimenez-Gomez A, Cordero-Guevara J. The association between sleep apnea and the risk of traffic accidents. *N Engl J Med* 1999;340:847–851.
- Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: Cross-sectional results of the Sleep Heart Health Study. *Am J Respir Crit Care Med* 2001;163:19–25.
- Babu AR, Herdegen J, Fogelfeld L, Shott S, Mazzone T. Type 2 diabetes, glycemic control, and continuous positive airway pressure in obstructive sleep apnea. *Arch Intern Med* 2005;165:447–452.
- Yaffe K, Laffan AM, Harrison SL, Redline S, Spira AP, Ensrud KE, Ancoli-Israel S, Stone KL. Sleep-disordered breathing, hypoxia, and risk of mild cognitive impairment and dementia in older women. *JAMA* 2011;306:613–619.
- Ensrud KE, Blackwell TL, Ancoli-Israel S, et al. Sleep disturbances and risk of frailty and mortality in older men. *Sleep Med* 2012;13:1217–1225.
- Centers for Disease Control and Prevention CDC. HIV surveillance report, 2011. Vol. 23, 2013.
- Epstein LJ, Strollo PJ Jr, Donegan RB, Delmar J, Hendrix C, Westbrook PR. Obstructive sleep apnea in patients with human immunodeficiency virus HIV disease. *Sleep* 1995;18:368–376.
- Schulz R, Lohmeyer J, Seeger W. Obstructive sleep apnea due to HIV-associated lipodystrophy. *Clin Infect Dis* 2003;37:1398–1399.
- Lo Re V 3rd, Schutte-Rodin S, Kostman JR. Obstructive sleep apnoea among HIV patients. *Int J STD AIDS* 2006;17:614–620.
- Brown TT, Patil SP, Jacobson LP, et al. Anthropometry in the prediction of sleep disordered breathing in HIV-positive and HIV-negative men. *Antivir Ther* 2010;15:651–659.
- Kunisaki K, Akgün K, Fiellin D, et al. Prevalence and correlates of obstructive sleep apnoea among patients with and without HIV infection. *HIV Med* 2015;16:105–113.
- Hoddinott SN, Bass MJ. The Dillman total design survey method. *Can Fam Physician* 1986;32:2366–2368.
- Johns MW. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep* 1991;14:540–545.
- Butt Z, Lai J, Rao D, Heinemann AW, Bill A, Cella D. Measurement of fatigue in cancer, stroke, and HIV using the Functional Assessment of Chronic Illness Therapy—Fatigue FACIT-F scale. *J Psychosom Res* 2013;74:64–68.
- Cella D, Yount S, Sorensen M, Chartash E, Sengupta N, Grober J. Validation of the Functional Assessment of Chronic Illness Therapy Fatigue Scale relative to other instrumentation in patients with rheumatoid arthritis. *J Rheumatol* 2005;325:811–819.
- Chung F, Yegneswaran B, Liao P, Chung SA, Vairavanathan S, Islam S, Khajehdehi A, Shapiro CM. STOP

- questionnaire: A tool to screen patients for obstructive sleep apnea. *Anesthesiology* 2008;108:812–821.
28. Heaton RK, Clifford DB, Franklin DR, Jr, et al. and CHARTER Group. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER Study. *Neurology* 2010;75:2087–2096.
 29. Breitbart W, McDonald MV, Rosenfeld B, Monkman ND, Passik S. Fatigue in ambulatory AIDS patients. *J Pain Symptom Manage* 1998;15:159–167.
 30. Sullivan PS, Dworkin MS, HIV Disease Investigators. Prevalence and correlates of fatigue among persons with HIV infection. *J Pain Symptom Manage* 2003;25:329–333.
 31. Rubinstein ML, Selwyn PA. High prevalence of insomnia in an outpatient population with HIV infection. *J Acquired Immune Defic Syndr Hum Retrovirol* 1998;19:260–265.
 32. Allavena C, Guimard T, Billaud E, et al. Prevalence and risk factors of sleep disturbances in a large HIV-infected adult population. *J Int AIDS Soc* 2014;17:19576.
 33. Salahuddin N, Barroso J, Leserman J, Harmon JL, Pence BW. Daytime sleepiness, nighttime sleep quality, stressful life events, and HIV-related fatigue. *J Assoc Nurses AIDS Care* 2009;20:6–13.
 34. Patil SP, Brown TT, Jacobson LP, et al. Sleep disordered breathing, fatigue, and sleepiness in HIV-infected and uninfected men. *PloS ONE* 2014;9:e99258.
 35. Crum-Cianflone N, Tejdor R, Medina S, Barahona I, Ganesan A. Obesity among patients with HIV: The latest epidemic. *AIDS Patient Care STDS* 2008;22:925–930.
 36. Babson KA, Heinz AJ, Bonn-Miller MO. HIV medication adherence and HIV symptom severity: The roles of sleep quality and memory. *AIDS Patient Care STDS* 2013;27:544–552.
 37. Dittner AJ, Wessely SC, Brown RG. The assessment of fatigue: A practical guide for clinicians and researchers. *J Psychosom Res* 2004;56:157–170.
 38. Ferrando S, Evans S, Goggin K, Sewell M, Fishman B, Rabkin J. Fatigue in HIV illness: Relationship to depression, physical limitations, and disability. *Psychosom Med* 1998;60:759–764.
 39. Rope AM, Fitch KV, Stanley TL, Looby SED, Grinspoon SK. Relationship between neck circumference and cardio-metabolic parameters in HIV-infected and non-HIV-infected adults. *Diabetes Care* 2011;34:1026–1031.
 40. Wirth MD, Jagers JR, Dudgeon WD, et al. Association of markers of inflammation with sleep and physical activity among people living with HIV or AIDS. *AIDS Behav* 2015;19:1098–1107.
 41. Wang T, Jiang Z, Hou W, et al. HIV Tat protein affects circadian rhythmicity by interfering with the circadian system. *HIV Med* 2014;15:565–570.
 42. Lee KA, Gay C, Humphreys J, Portillo CJ, Pullinger CR, Aouizerat BE. Telomere length is associated with sleep duration but not sleep quality in adults with human immunodeficiency virus. *Sleep* 2014;37:157–166.
 43. Hiestand DM, Britz P, Goldman M, Phillips B. Prevalence of symptoms and risk of sleep apnea in the US population. Results from the National Sleep Foundation Sleep in America 2005 Poll. *Chest* 2006;130:780–786.
 44. Larsson L, Lindberg A, Franklin KA, Lundbäck B. Gender differences in symptoms related to sleep apnea in a general population and in relation to referral to sleep clinic. *Chest* 2003;124:204–211.
 45. Young T, Hutton R, Finn L, Badr S, Palta M. The gender bias in sleep apnea diagnosis: Are women missed because they have different symptoms? *Arch Intern Med* 1996;156:2445–2451.
 46. Durán J, Esnaola S, Rubio R, Iztueta Á. Obstructive sleep apnea–hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 yr. *Am J Respir Crit Care Med* 2001;163:685–689.

Address correspondence to:

Ken Kunisaki, MD, MS
 Department of Pulmonary,
 Critical Care and Sleep Apnea (111N)
 University of Minnesota
 One Veterans Drive
 Minneapolis, MN, 55417

E-mail: kunis001@umn.edu