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Authors

Orr, Jeremy E

Velazquez, Jazmin

Schmickl, Christopher N

et al.

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Sleep, Sleep Apnea, and Fatigue in People Living With HIV

Jeremy E. Orr, MD[a], **Jazmin Velazquez, BA**[a], **Christopher N. Schmickl, MD, PhD**[a], **Naa-Oye Bosompra, BA**[a], **Pamela N. DeYoung, BA, RPSGT**[a], **Dillon Gilbertson, MS**[a], **Atul Malhotra, MD**[a], **Igor Grant, MD**[b], **Sonia Ancoli-Israel, PhD**[b], **Maile Young Karris, MD**[c], **Robert L. Owens, MD**[a]

[a]Division of Pulmonary, Critical Care and Sleep Medicine, University of California San Diego, San Diego, CA

[b]Department of Psychiatry, University of California San Diego, San Diego, CA

[c]Divisions of Infectious Diseases & Global Public Health and Geriatrics & Gerontology, University of California San Diego, San Diego, CA.

Abstract

Background: People living with HIV (PLWH) often report fatigue even when viral load is suppressed. Obstructive sleep apnea (OSA), which is often associated with fatigue, is common in PLWH, but whether OSA explains fatigue in this population is unknown.

Setting: Academic university-affiliated HIV and Sleep Medicine Clinics.

Methods: PLWH, aged 18–65 years, with a body mass index of 20–35 kg/m^2 and viral suppression (RNA <200 copies per mL), were recruited to undergo daytime questionnaires, including the Functional Assessment of Chronic Illness Therapy Fatigue Scale and Epworth Sleepiness Scale, 7 days of actigraphy (to determine daily sleep duration and activity amplitude and rhythms), and an in-laboratory polysomnography to assess for the presence and severity of OSA.

Results: Of 120 subjects with evaluable data, 90 (75%) had OSA using the American Academy of Sleep Medicine 3% desaturation or arousal criteria, with an apnea–hypopnea index >5/h. There was no difference in Functional Assessment of Chronic Illness Therapy scores between those with and without OSA, although those with OSA did report more daytime sleepiness as measured using the Epworth Sleepiness Scale. In a multivariable model, predictors of fatigue included more variable daily sleep durations and decreased mean activity counts. Sleepiness was predicted by the presence of OSA.

Conclusion: OSA was very common in our cohort of PLWH, with those with OSA reporting more sleepiness but not more fatigue. Variability in sleep duration was associated with increased

Correspondence to: Robert L. Owens, MD, University of California San Diego, 9300 Campus Point Drive, La Jolla, CA 92037(rowens@health.ucsd.edu).

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The manuscript reports data from a clinical trial, which has been registered on ClinicalTrials.gov as "Obstructive Sleep Apnea Endotypes and Impact on Phenotypes of People Living With HIV (PLWH/OSA)" with NCT03575143.

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fatigue. Further study is needed to determine if treatment of OSA, or an emphasis on sleep consistency and timing, improves symptoms of fatigue in PLWH.

Keywords

obstructive sleep apnea; fatigue; HIV; people living with HIV

INTRODUCTION

Treatment of HIV with antiretroviral therapy (ART) has dramatically reduced progression to AIDS and death.[1] Today, because an increasing number of people living with HIV (PLWH) are living longer, there is a new emphasis on management of symptoms and comorbidities. Fatigue is one of the most prominent symptoms, affecting ~50% of PLWH even when viral load is suppressed and normal CD4 counts are achieved.[2,3] Fatigue in the context of HIV is further associated with functional impairments specifically interfering with instrumental activities of daily living, work, family, and social interactions.[4]

Fatigue in PLWH has been attributed to a variety of causes: chronic inflammation from HIV and other active infections, adverse effects of ART (eg, efavirenz, among others), comorbid psychiatric disorders, and substance use. Perhaps because fatigue is such a prevalent symptom, obstructive sleep apnea (OSA) as a potential cause is only occasionally considered despite its association with fatigue.[5] Several lines of reasoning suggest that suboptimal sleep and/or OSA play a role in fatigue for PLWH.[6] First, sleep problems are a long recognized and frequently reported symptom in PLWH and, as such, are included in the HIV symptom index.[7–9] Studies evaluating the sleep patterns of PLWH reveal subjective difficulty with falling and staying asleep with more objective measurements using actigraphy demonstrating that sleep is often short (<6 hours) and fragmented. Second, witnessed apnea, a fairly specific marker of OSA, is a predictor for clinically relevant fatigue in PLWH.[10] Third, studies suggest that OSA is common in PLWH despite few being evaluated and even fewer treated.[11–13]

Punjabi and colleagues also found that there was a slightly higher prevalence of OSA in PLWH compared with that in matched controls without HIV, perhaps suggesting that HIV is a risk factor of OSA.

To our knowledge, few studies have comprehensively assessed the role of sleep duration and OSA on fatigue in PLWH. We hypothesized that fatigue is overexpressed in PLWH with OSA (PLWH+OSA) compared with PLWH without OSA (PLWH-OSA), independent of known covariates.

METHODS

Study Design

We performed a prospective cohort study of PLWH (NCT03575143). The study was approved by the UCSD Human Research Protection Program (#180160), and all participants provided written informed consent.

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Participants

Eligible participants were those living with HIV and viral suppression (RNA <200 copies/mL), aged 18–65 years, body mass index (BMI) 20–35 kg/m^2. Participants were recruited through physician referrals, interest forms, support groups, and clinic-based flyers in San Diego. Those recruited were English language speakers (based on the ability to complete all study questionnaires). Exclusion criteria included pregnancy, currently adherent to effective treatment for OSA, and other noninsomnia sleep fragmenting disorders (eg, periodic limb movement disorder or narcolepsy).

Data Collection and Questionnaires

During the baseline visit, demographic data, medical history focused on comorbidities, current and past ART medications, the use of opioids, and depression symptom scores using the Beck Depression Inventory II scale were collected. Fatigue was assessed with the Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F, primary outcome), and daytime sleepiness was assessed with the Epworth Sleepiness Scale (ESS). Objective sleep was measured both with actigraphy and polysomnography.

The Facit-F is a 13-item questionnaire designed to assess self-reported fatigue and its impact on daily activity and function.[14,15] All 13 items are equally weighted and scored on a scale of 0–4, 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. Normative data have been reported in PLWH.[10,16] The ESS measures subjective daytime sleepiness by asking participants their likelihood of falling asleep in 8 different scenarios. All 8 items are equally weighted and scored on a scale of 0–3, yielding a total score of 0–24, with scores ≥11 denoting excessive daytime sleepiness.[17] Because prior reports emphasized the link between fatigue and witnessed apneas, we also assessed for signs/symptoms of OSA using the STOP-BANG questionnaire.[18]

Actigraphy Collection and Analysis

Participants were given wrist-worn actigraphs (Actiwatch Spectrum Pro, Philips Respironics) to wear for 7 consecutive days on their nondominant hand and were asked to complete a daily diary (which was used to help edit the data). The actigraphy devices acquired continuous measurements of activity and provided activity values in 15-second epochs. Actigraphy data were used to compute sleep duration and circadian activity rhythms.

For sleep duration, output was manually reviewed by an experienced scorer to define “rest intervals,” in which the participant was thought to be sleeping; the scorer also designated nighttime (or main) or naptime rest intervals (defined as at least 10 minutes of no activity) incorporating details from the daily diary, as needed. Within these rest intervals, the software algorithm defined each epoch as “sleep” versus “wake,” using a threshold of “Medium” within the software, which translates to an activity count of 40 within an epoch to be considered awake. For each subject, we also calculated the SD of total sleep duration per day.

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Average total sleep time per 24 hours (over the recording period) was calculated and further divided into nighttime sleep (ie, sleep that occurred as the main sleep period) and naps (sleep that occurred outside the main sleep period).

For circadian activity rhythms, activity counts per 1-minute epoch were fitted to a cosinor regression model to calculate circadian metrics. Using the cosinor2 package[19] in the R environment (R v. 4.1.1), a cosinor regression model was applied to each day of data using a period of 24 hours (midnight to midnight) with 1-minute epochs. This enabled the extraction of the following daily metrics[20]:

- *MESOR.* Mean activity count per minute.
- *Amplitude.* Vertical distance (in activity counts) from the MESOR to the peak of the cosine wave.
- *Acrophase.* Time of the peak of activity, using a 24-hour clock, on the cosine wave.
- R^2. Goodness-of-fit value from the regression model.

We note that what is described here refers to a circadian activity pattern based on actigraphy and not the patients' biologic circadian rhythm—for example, that which might be measured with recording periods independent from other circadian cues or serum melatonin levels.

Polysomnography

Participants underwent in-laboratory, attended polysomnography (PSG; Nihon Kohden America, Irvine, CA) to assess the presence and severity of OSA. Subjects were instrumented in the standard fashion with electroencephalogram, electrooculogram, and chin electromyogram for sleep staging; nasal pressure transducer and thermistor for air flow; respiratory impedance belts at the thorax and abdomen for respiratory effort; electrocardiogram for heart rate; and pulse oximetry. Studies were scored by a single experienced registered PSG technologist. The apnea–hypopnea index (AHI) was primarily quantified using American Academy of Sleep Medicine (AASM) recommended criteria "AHI3A" (ie, 1A criteria—hypopnea defined as a >30% decrement in nasal pressure with 3% desaturation and/or an arousal). In addition, we quantified the "AHI4" based on the AASM acceptable criteria (ie, 1B, "Medicare"—hypopnea as >30% decrease in nasal pressure with 4% desaturation). OSA severity was categorized as mild (AHI 5–15/h), moderate (AHI 15–30/h), and severe (AHI >30/h).

Reference Standard

There is increasing evidence that even patients with mild OSA that is associated with arousals rather than hypoxemia (ie, AHI3A 5–15/h) have attributable symptoms and can substantially benefit from OSA therapy regarding daytime sleepiness, fatigue, and low energy.[21,22] Thus, for the primary analysis, we used "any OSA" based on the recommended criterion (ie, AHI3A ≥5/h) as the reference standard. For secondary analyses, we further used the AHI4 ≥5/h and the AHI3A/AHI4 ≥15/h (ie, moderate-severe OSA) as reference standards.

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Sample Size and Statistical Analyses

Based on published literature, we had expected a 50% prevalence of OSA (defined as an AHI >5/h using 4% criteria). Based on prior FACIT-F scores in HIV, our planned sample size of 120 demonstrated an 80% statistical power to detect a minimal clinically important difference of 3 points between the 2 groups. Power is based on a two-sided, two-sample *t* test, assuming that alpha is set to 0.05. To account for 10% attrition, we planned to enroll 134 subjects to achieve 120 evaluable subjects.

Statistical analyses were performed using R (3.6.1), using *P* values <0.05 to denote statistical significance. Descriptive statistics are reported as noted in the text and tables. The primary outcome was the FACIT-F–derived fatigue score, with ESS as the main secondary outcome. Differences across OSA strata were evaluated using one-way ANOVA. A multivariable model of sleep variables was constructed to evaluate focal variables of interest from PSG (AHI) and actigraphy (mean sleep duration, mean sleep duration SD, sleep efficiency; acrophase, MESOR, amplitude) while adjusting for covariates (age, sex) based on prior literature. In prior literature, opioid use, depression, and antiretroviral therapy regimens have been associated with fatigue, and we explored the impact of BMI on fatigue and sleepiness. We examined these relationships by creating 4 additional models in which we individually incorporated each of these variables in addition to the multivariable sleep model.

RESULTS

Participants

A total of 131 PLWH met eligibility criteria and were enrolled in the study; 120 subjects completed all of the study procedures, with demographic data listed in Table 1. Participants were of middle age, predominantly men and over-weight, with a diverse racial background and ethnicity (25% Hispanic). Twenty-two participants reported a prior diagnosis of OSA but were not currently on any therapy such as continuous positive airway pressure. Most (71%) subjects were on an integrase nonstrand transfer inhibitor (INSTI) drug regimen.

PSG OSA Results

Based on an AHI3A >5/h, OSA was present in 90 (75%) participants (29 mild, 19 moderate, and 42 severe). As described above, using a more conservative definition that relies on greater oxygen desaturation levels (AHI4% >5/h), 69 participants (58%) met OSA criteria (24 mild, 16 moderate, and 29 severe). As might be expected, those with OSA using either definition were older and had a higher BMI compared with those without OSA.

Fatigue and Sleepiness

In unadjusted analysis, FACIT-F scores were not different across OSA strata (one-way ANOVA, $P = 0.94$; Table 2, Fig. 1) or when comparing PLWH+OSA (ie, AHI3A >5/h) and PLWH-OSA (ie, AHI3A <5/h) groups [median 35 IQR (26–43) vs 34 (25–46); $P = 0.70$]. Sleepiness assessed by ESS was not different across OSA strata ($P = 0.38$; Table 2, Fig. 1) but was greater in PLWH+OSA than in PLWH-OSA [median 8 (IQR 5–12) vs $7^{5,8}$; $P =$

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0.031]. We also examined the relationship between fatigue and OSA status using AHI4% criteria, and there was also no relationship between fatigue and OSA status (data not shown).

Despite differences in the patterns of FACIT-F scores and ESS, there was a statistically significant inverse relationship between the 2; more fatigue was associated with greater sleepiness (beta = 21.0 [95% CI 21.4 to 20.59]; $P < 0.001$; ie, 1-point increase in ESS [more sleepy] is associated with a 1-point decrease in FACIT [worse fatigue]; Figure 2).

Other nonsleep factors associated with increased fatigue were concomitant opioid use, use of non-INSTI ART regimen, and greater symptoms of depression (see Figure 1, Supplemental Digital Content, http://links.lww.com/QAI/C320). Those on an INSTI drug regimen had less fatigue (median FACIT score was 36 [IQR 29–45] vs. 26 [IQR 17–40]; $P = 0.003$ on non-INSTI regimen). Body mass index was not associated with fatigue. Only depression symptoms were associated with increased tiredness as assessed by ESS, not opioid use, ART regimen, or BMI.

Actigraphy

Because of data loss (unrelated to OSA status or other examined variables), full actigraphy data were available in 77 of 120 subjects. Total sleep times and other metrics are reported in Table 1. There were no differences between those with and without OSA related to sleep durations or other circadian activity metrics, although one-way ANOVA did detect differences between OSA strata (Table 2) in mean activity during the day (MESOR) and amplitude.

Multivariable Sleep Model

Using a multivariable model, the presence of OSA was not associated with a lower FACIT score. Instead, more variable sleep durations (as assessed by the SD of sleep times), lower average activity counts (MESOR), and greater amplitude independently predicted a greater burden of fatigue (see Fig. 3A). Regarding sleepiness, the presence of OSA was the only statistically significant predictor (see Fig. 3B).

Nonsleep factors such as opioid use, ART regimen, and depression symptoms were examined when added individually to the sleep model, and all were statistically associated with fatigue scores. MESOR and amplitude remained significantly associated with fatigue, whereas sleep duration variability only demonstrated borderline significance (P values ranging from 0.059 to 0.11 across the 3 models). For sleepiness, only depression symptoms were statistically important, and when incorporated in the model, they reduced the statistical significance of the relationship between OSA and sleepiness ($P = 0.10$). Although body mass index was not statistically important, its incorporation in the model also diminished the impact of OSA on sleepiness ($P = 0.09$).

DISCUSSION

Although we found that OSA was highly prevalent in our cohort of PLWH, there was no difference in fatigue, as measured by FACIT-F between participants with and without OSA. However, PLWH+OSA reported greater sleepiness compared with PLWH-OSA. These

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findings suggest that OSA contributes to sleepiness but not fatigue in PLWH. Nonetheless, the language of these 2 symptoms is related and may be difficult to distinguish in some patients in clinical practice.[23] Thus, because the treatment of OSA may improve fatigue and energy levels, people with OSA who reference terms other than sleepiness may still benefit from OSA treatment.[5,24,25]

To put our results in context, we note that the fatigue scores in our cohort are still low compared with those in the general population (median FACIT score 47).{Cella, 2002 #1270} The values we observed in our cohort are more similar to those with other chronic diseases such as rheumatoid arthritis.{Cella, 2005 #296} Thus, it is also possible that the contribution of HIV to fatigue is much greater than any contribution of OSA to fatigue. Unfortunately, FACIT data are not available for those with OSA alone, but further studies might reveal an impact of OSA on fatigue in non-HIV (ie, less overall fatigued) populations. Prior data are somewhat mixed regarding OSA and fatigue. Although Goswami and colleagues have reported worse FACIT scores with witnessed apneas (a specific although not sensitive marker of OSA), Patil and colleagues also did not find the presence of objectively measured OSA to be associated with subjective fatigue (although not using FACIT).{Goswami, 2015 #242; Patil, 2014 #4}

Punjabi et al.[13] reported a very high prevalence of OSA in men living with HIV (75%), consistent with what we observed in our study, which also included women. Here, we build on that work by demonstrating the association of OSA with specific symptoms such as sleepiness. Goswami and colleagues previously demonstrated that witnessed apneas were associated with fatigue; however, the number of participants who reported witnessed apneas was much lower (;25%) than the OSA prevalence we found.[10] Of note, the FACIT fatigue questionnaire has several questions that relate to tiredness and even need for sleep during the day. We did find that ESS was correlated with fatigue, although the association was not robust (see Fig. 2). Thus, although fatigue, sleepiness, or other symptoms, such as tiredness, lack of motivation, etc, are closely related and sometimes used interchangeably, they appear to have unique underlying causes. Although we have focused on our novel sleep data, our data confirmed other important associations with fatigue such as medications and symptoms of depression.

In a multivariate model, we found that several parameters derived from actigraphy were associated with increased fatigue. Perhaps surprisingly, sleep duration did not predict fatigue, although many subjects had short sleep duration. This finding might be a limitation of the use of actigraphy in that longer apparent sleep times might reflect sleep and then periods of wake but little activity, ie, actigraphy may over-estimate total sleep time.[26] Also, those with long sleep times might have other comorbid diseases that could also contribute to fatigue such as depression.[27] Regardless, we emphasize that treatment of short sleep duration and sleep-disordered breathing might still offer benefits regarding fatigue (and other symptoms) in PLWH. Variability in sleep duration did predict fatigue. Increasingly, sleep variability (not just sleep duration) is being investigated because it is associated with greater body mass index, cardiac disease, and even mortality.[28–30] Thus, timing and regularity of sleep might represent a modifiable risk factor of overall health but also symptoms of fatigue.

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The largest effects appeared to relate to associations between circadian activity rhythms and fatigue. Similar to prior studies using self-reported activity levels, we also found that increased physical activity on average (based on MESOR, the mean of the rhythm) was associated with decreased fatigue.[31] Other circadian activity metrics such as a delayed acrophase (circadian timing) were correlated with fatigue although not reaching statistical significance. Whether these differences in activity timing reflect underlying genotype, the endogenous circadian rhythm, or a modifiable risk factor of fatigue is unclear.[32] We note that morning bright light therapy has been effective at reducing fatigue in other groups with chronic illness.[33–35]

We confirmed prior associations between fatigue and nonsleep factors. As previously reported, we also found that the use of opioids and depression were associated with increased fatigue.{Goswami, 2015 #242} Only a single subject in our study used efavirenz. Interestingly, we did find that those on an INSTI ART regimen—consistent with current guidelines—had substantially less fatigue than those on other therapies.{Gandhi, 2023 #1272} As found in other literature, increased depression symptoms were associated with increased tiredness.{Garbarino, 2020 #1271} Thus, although sleep interventions might ultimately be useful to reduce fatigue in PLWH, other possible interventions might be changes in medications and/or assessment and treatment of depression.

Strengths of this study include the rigorous objective measurements of OSA and sleep parameters of PLWH. Limitations include the relatively modest sample size that may have limited our ability to determine correlations between secondary outcomes. As with all studies relying on ambulatory actigraphy, total sleep time is likely slightly overestimated compared with actual sleep time.[26] In addition, our estimates of circadian timing are based on activity and may not reflect the underlying biology.

In conclusion, OSA was common in PLWH and contributed to subjective sleepiness but not clearly to fatigue. Future studies examining the impact of interventions to treat OSA, regularize sleep schedule, and improve circadian timing (eg, bright light therapy) on fatigue and sleepiness are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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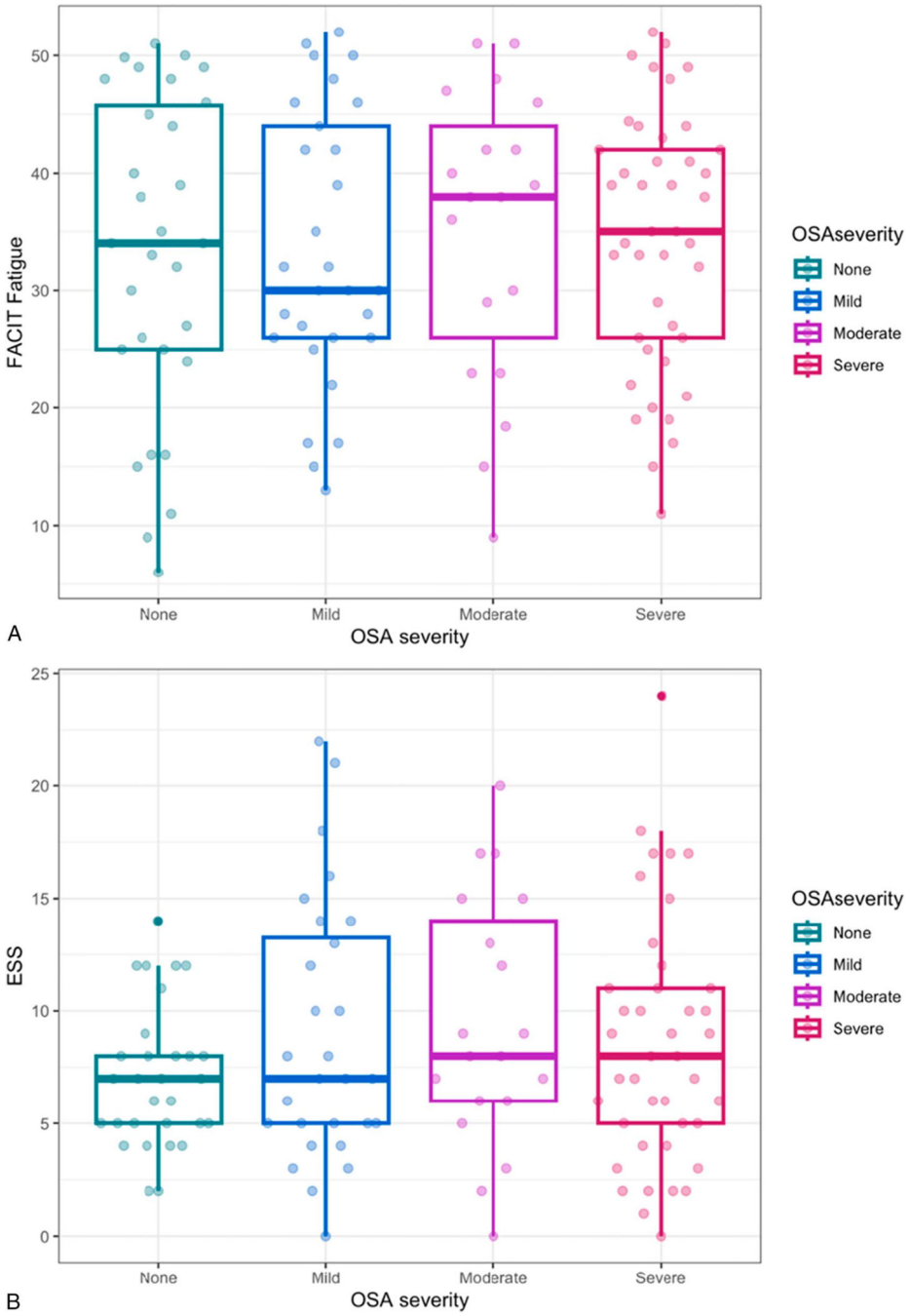

FIGURE 1.

A, Fatigue scores by OSA severity based on sleep apnea severity. Lower FACIT scores indicate greater symptoms of fatigue. B, Subjective sleepiness based on sleep apnea severity. Higher Epworth (ESS) scores indicate greater sleepiness.

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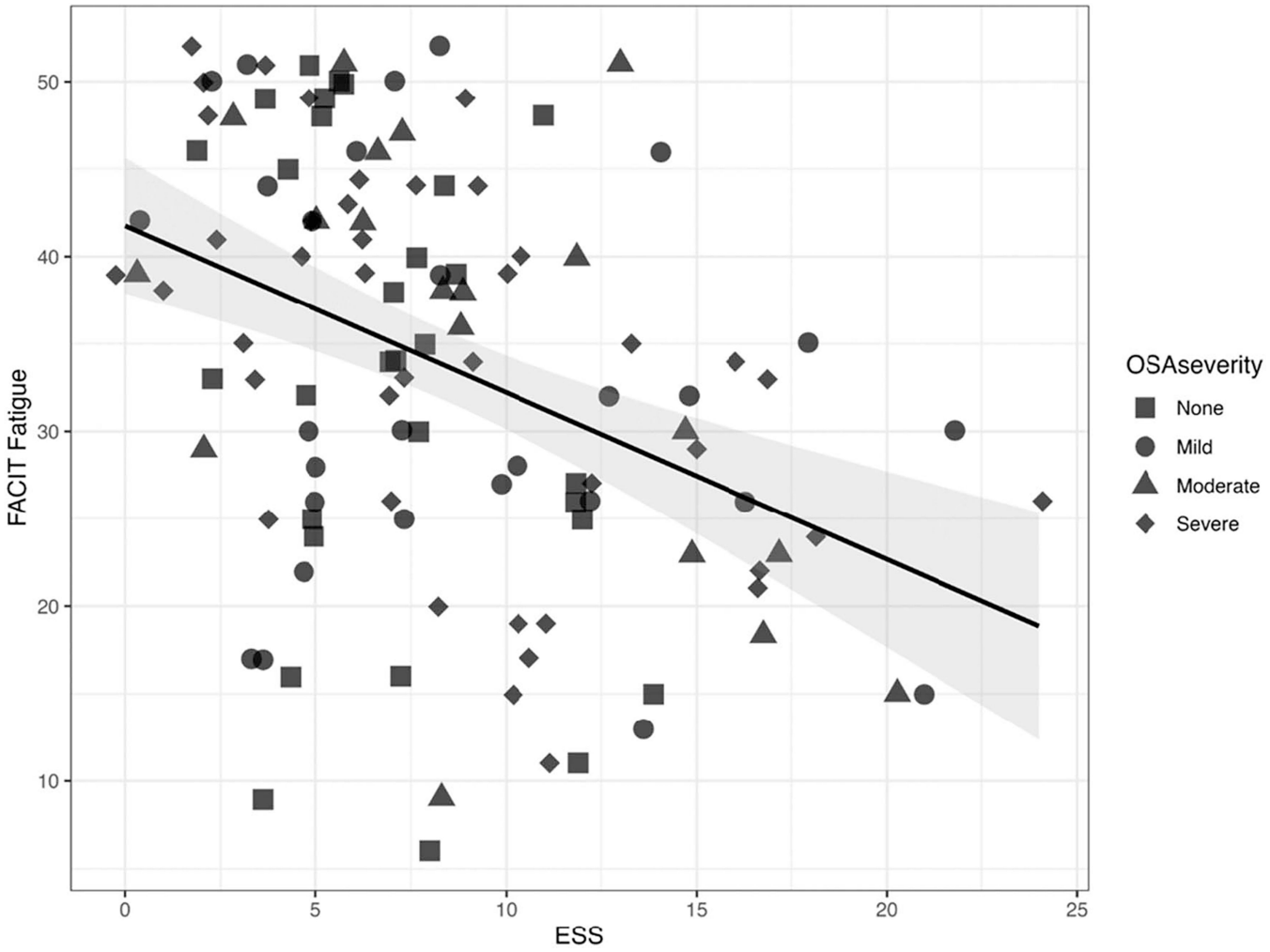

FIGURE 2.
Relationship between subjective tiredness and fatigue (higher ESS score reflects worse sleepiness; lower FACIT score suggests worse fatigue).

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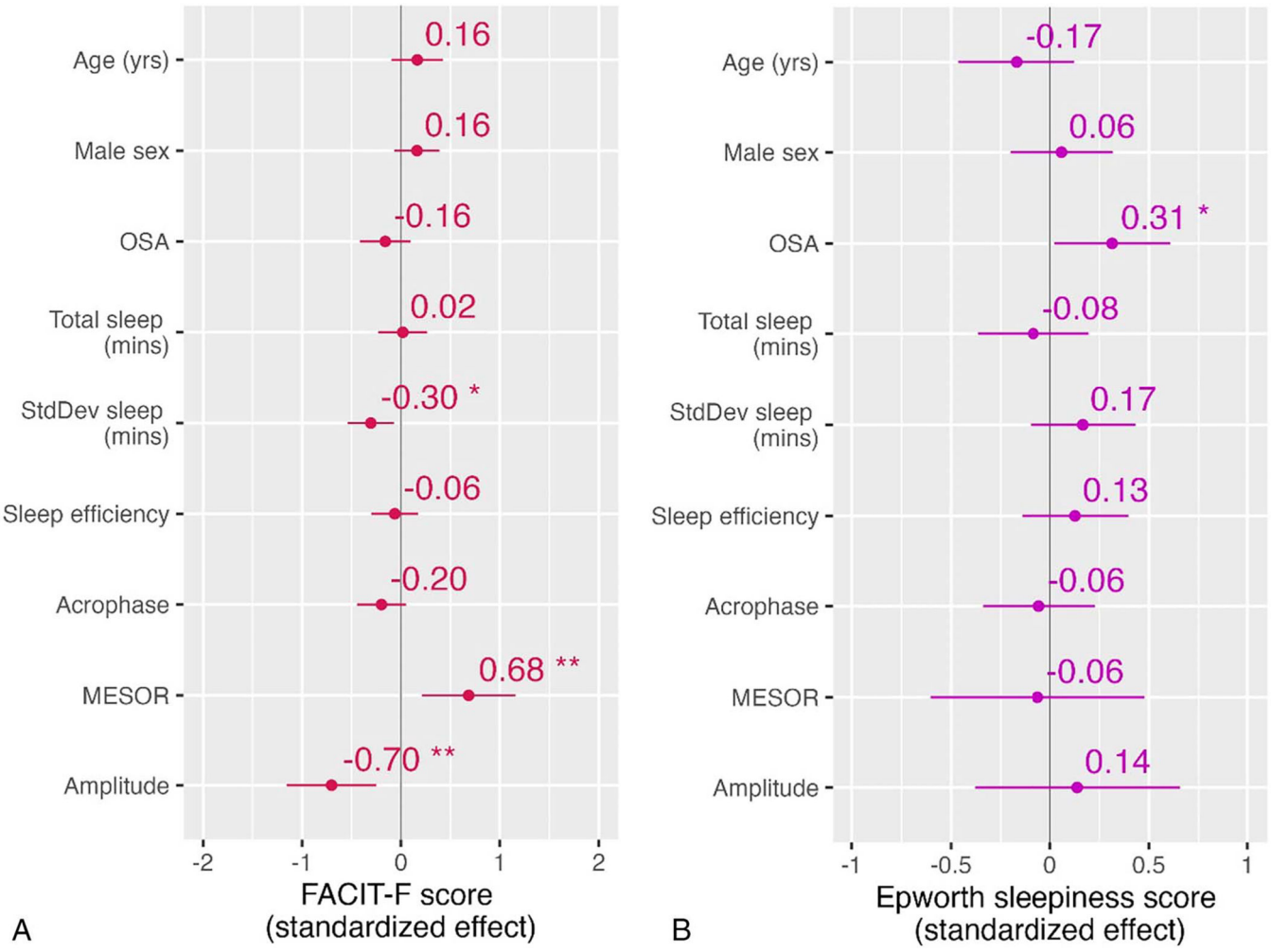

FIGURE 3.

Multivariate sleep model factors associated with (A) FACIT-F score and (B) ESS with beta and confidence intervals. **P*, 0.05, ***P*, 0.01, and ****P*, 0.001. For FACIT-F score, a higher score suggests less fatigue. For ESS, a higher score indicates more sleepiness.

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TABLE 1.

Demographic, Questionnaire, Polysomnographic, and Actigraphy Data by OSA Status Using AHI3% >5/h

	No OSA, N = 30*	OSA, N = 90*	*P* †
Age (yr)	46 (32–53) [26–62]	54 (47–58) [24–65]	0.001
Male sex	24 (80)	78 (87)	0.39
BMI (kg/m^2)	25.4 (22.0–28.6) [20.1–34.1]	27.4 (25.5–29.7) [17.8–34.9]	0.016
Non-Hispanic	24 (80)	66 (73)	0.47
Race			0.33
American Indian/Alaska Native	1 (3.3)	4 (4.4)	
Asian	1 (3.3)	0 (0)	
Native Hawaiian or other Pacific Islander	0 (0)	1 (1.1)	
Black or African American	6 (20)	13 (14)	
White	15 (50)	60 (67)	
More than one race	6 (20)	10 (11)	
Unknown/not reported	1 (3.3)	2 (2.2)	
Opioid medications	4 (13)	15 (17)	0.78
Sleep medications	14 (47)	40 (44)	0.83
Smoking?			0.60
Never	10 (37)	40 (48)	
Past	9 (33)	23 (28)	
Current	8 (30)	20 (24)	
Unknown	3	7	
INSTI ART regimen	22 (73)	65 (73)	0.97
Total AHI3% (per h)	3 (2–4) [1–5]	27 (13–50) [5–103]	<0.001
AHI4% (per h)	1 (1–2) [0–3]	14 (6–39) [0–102]	<0.001
NREM AHI3% (per h)	3 (2–4) [1–40]	25 (11–50) [1–103]	<0.001
REM AHI3% (per h)	4 (2–7) [0–22]	27 (13–56) [0–120]	
No REM observed	0	1	<0.001
Total sleep duration, PSG (min)	359 (325–400) [279–484]	338 (298–376) [153–506]	0.065
N1 duration (min)	34 (22–40) [12–95]	52 (36–81) [12–207]	<0.001
N2 duration (min)	220 (181–250) [110–388]	177 (150–211) [15–355]	0.002

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	No OSA, N = 30*	OSA, N = 90*	P †
N3 duration (min)	20 (8–53) [0–141]	19 (2–51) [0–129]	0.52
Total REM duration (min)	64 (52–74) [4–140]	60 (38–84) [0–150]	0.69
FACIT-F	34 (25–46) [6–51]	35 (26–43) [9–52]	0.70
Epworth Sleepiness Scale	7 (5–8) [2–14]	8 (5–12) [0–24]	0.036
Unknown	0	2	
Beck Depression Inventory II	13 (8–23) [2–39]	13 (4–21) [0–47]	0.17
Unknown	0	4	
Actigraphy-derived 24-h sleep mean duration (min)	439 (401–470) [276–530]	422 (368–468) [177–605]	0.58
Unknown	11	32	
Actigraphy-derived 24-h sleep SD (min)	82 (53–145) [20–292]	74 (61–131) [16–319]	0.77
Unknown	11	32	
Sleep efficiency (%)	85 (78–91) [66–98]	84 (76–90) [41–99]	0.17
	11	32	
Corrected acrophase (h)	15.33 (13.93–17.00) [12.55–19.57]	14.91 (13.94–16.04) [9.14–18.69]	0.27
Unknown	11	35	
MESOR (activity counts)	94 (74–107) [44–140]	78 (61–103) [36–212]	0.30
Unknown	11	35	
Amplitude estimate	71 (50–81) [22–92]	55 (43–82) [14–219]	0.92
Unknown	11	35	
R fit	0.66 (0.57–0.71) [0.34–0.82]	0.67 (0.58–0.704) [0.29–0.890]	0.53
Unknown	11	35	

*Median (IQR) [range]; n (%).

†Welch two-sample *t* test; Fisher exact test; Pearson x^2 test.

ART INSTI, antiretroviral regimen using integrase nonstrand transfer inhibitor; N1, NREM stage 1 sleep; NREM, non–rapid eye movement sleep; REM, rapid eye movement sleep.

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TABLE 2.

Demographic, Questionnaire, Polysomnographic, and Actigraphy Data by OSA Strata

	No OSA, N = 30*	Mild OSA, N = 29*	Moderate OSA, N = 19*	Severe OSA, N = 42*	*P* †
Age (yr)	46 (32–53) [26–62]	47 (39–56) [25–65]	57 (53–61) [24–64]	55 (51–58) [29–64]	<0.001
Male sex	24 (80)	19 (66)	18 (95)	41 (98)	0.001
BMI (kg/m^2)	25.4 (22.0–28.6) [20.1–34.1]	27.4 (25.0–30.8) [21.6–34.3]	26.0 (23.6–28.4) [17.8–34.9]	28.0 (26.3–29.3) [23.0–34.0]	0.010
Non-Hispanic	24 (80)	21 (72)	15 (79)	30 (71)	0.806
Race					
American Indian/Alaska Native	1 (3.3)	0 (0)	1 (5.3)	3 (7.1)	
Asian	1 (3.3)	0 (0)	0 (0)	0 (0)	
Native Hawaiian or other Pacific Islander	0 (0)	0 (0)	0 (0)	1 (2.4)	
Black or African American	6 (20)	6 (21)	0 (0)	7 (17)	
White	15 (50)	18 (62)	16 (84)	26 (62)	
More than one race	6 (20)	5 (17)	2 (11)	3 (7.1)	
Unknown/Not reported	1 (3.3)	0 (0)	0 (0)	2 (4.8)	
Opioid medications	4 (13)	4 (14)	5 (26)	6 (14)	0.618
Sleep medications	14 (47)	11 (38)	10 (53)	19 (45)	0.856
Smoking?					0.656
Never	10 (37)	16 (59)	9 (50)	15 (38)	
Past	9 (33)	4 (15)	5 (28)	14 (36)	
Current	8 (30)	6 (22)	4 (22)	10 (26)	
Unknown	3	3	1	3	
INSTI ART regimen	22 (73)	21 (72)	15 (83)	29 (69)	0.744
Total AHI3% (per h)	3 (2–4) [1–5]	10 (8–12) [5–14]	20 (18–25) [17–30]	52 (41–70) [30–103]	<0.001
AHI4% (per h)	1 (1–2) [0–3]	4 (2–6) [0–11]	13 (10–17) [3–21]	42 (28–60) [4–102]	<0.001
NREM AHI3% (per h)	3 (2–4) [1–40]	8 (6–12) [1–16]	20 (15–23) [9–33]	51 (42–70) [25–103]	<0.001
REM AHI3% (per h)	4 (2–7) [0–22]	13 (5–18) [0–120]	34 (17–41) [7–65]	50 (26–66) [0–92]	<0.001
No REM observed	0	1	0	0	
Sleep efficiency (%)					
From PSG	85 (78–91) [66–98]	85 (78–91) [41–99]	84 (76–90) [64–98]	82 (74–87) [47–97]	0.326
Total sleep duration PSG (min)	359 (325–400) [279–484]	338 (298–404) [153–506]	338 (323–368) [253–473]	334 (290–374) [210–443]	0.255

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	No OSA, N = 30*	Mild OSA, N = 29*	Moderate OSA, N = 19*	Severe OSA, N = 42*	P †
N1 duration (min)	34 (22–40) [12–95]	45 (32–71) [12–111]	38 (28–51) [12–68]	78 (52–98) [21–207]	<0.001
N2 duration (min)	220 (181–250) [110–388]	189 (158–220) [37–355]	205 (180–227) [15–317]	166 (139–194) [99–264]	<0.001
N3 duration (min)	20 (8–53) [0–141]	29 (8–71) [0–129]	36 (10–48) [0–117]	7 (0–30) [0–102]	0.103
Total REM duration (min)	64 (52–74) [4–140]	60 (38–87) [0–150]	58 (41–80) [4–88]	62 (35–84) [0–136]	0.846
FACIT-F	34 (25–46) [6–51]	30 (26–44) [13–52]	38 (26–44) [9–51]	35 (26–42) [11–52]	0.899
Epworth sleepiness scale	7 (5–8) [2–14]	7 (5–13) [0–22]	8 (6–14) [0–20]	8 (5–11) [0–24]	0.354
Unknown	0	1	0	1	
Beck depression inventory II	13 (8–23) [2–39]	11 (4–21) [0–37]	12 (5–16) [1–38]	14 (5–21) [0–47]	0.514
Unknown	0	1	1	2	
Actigraphy-derived 24-h sleep mean duration (min)	494 (447–514) [337–583]	475 (421–554) [195–642]	475 (440–507) [404–587]	491 (428–531) [378–660]	0.998
Unknown	11	9	12	11	
Actigraphy-derived 24-h sleep SD (min)	91 (61–157) [25–331]	19 (76–138) [17–333]	78 (58–162) [29–298]	88 (73–179) [30–353]	0.924
Unknown	11	9	12	11	
Sleep efficiency (%)	0.90 (0.85–0.92) [0.81–0.94]	0.89 (0.86–0.91) [0.63–0.95]	0.85 (0.84–0.89) [0.72–0.90]	0.90 (0.87–0.91) [0.75–0.94]	0.414
	11	9	12	11	
Corrected acrophase (h)	15.33 (13.93–17.00) [12.55–19.57]	15.29 (14.33–16.62) [11.79–18.69]	14.26 (13.45–14.65) [12.46–16.00]	14.79 (14.03–16.02) [9.14–18.12]	0.248
Unknown	11	11	11	13	
MESOR (activity counts)	94 (74–107) [44–140]	66 (54–96) [36–153]	101 (84–133) [62–212]	78 (62–92) [36–136]	0.038
Unknown	11	11	11	13	
Amplitude estimate	71 (50–81) [22–92]	48 (41–63) [14–168]	79 (63–108) [40–219]	54 (43–79) [26–128]	0.047
Unknown	11	11	11	13	
R fit	0.66 (0.57–0.71) [0.34–0.82]	0.62 (0.57–0.70) [0.29–0.80]	0.73 (0.72–0.76) [0.47–0.90]	0.67 (0.58–0.76) [0.53–0.82]	0.119
Unknown	11	11	11	13	

*Median (IQR) [range]; n (%).

†One-way ANOVA; Fisher exact test; Pearson x^2 test.

ART INSTI, antiretroviral regimen using integrase nonstrand transfer inhibitor; N1, NREM stage 1 sleep; NREM, non–rapid eye movement sleep; REM, rapid eye movement sleep.