



# Comorbid insomnia and sleep apnea in Veterans with post-traumatic stress disorder

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## Abstract

**Purpose** The purpose of this study was to determine the impact of insomnia in Veterans with post-traumatic stress disorder (PTSD) and obstructive sleep apnea (OSA) on health-related outcomes before and after 12 weeks of continuous positive airway pressure (CPAP) treatment.

**Methods** We conducted a prospective cohort study of Veterans with PTSD and documented apnea hypopnea index (AHI)  $\geq 5$  with and without clinically significant insomnia as determined by the Insomnia Severity Index (ISI). Health-related outcomes including PTSD checklist (PCL-M), SF-36, and Pittsburgh Sleep Quality Index (PSQI) were assessed at baseline and 12 weeks after initiation of OSA treatment. CPAP adherence was retrieved at each visit.

**Results** Seventy-two Veterans including 36 with comorbid insomnia and OSA (COMISA) and 36 OSA-only were enrolled. Veterans with COMISA were younger ( $p = 0.03$ ), had lower BMI ( $p < 0.001$ ), and were more likely to report depression than those with OSA-only ( $p = 0.004$ ). Although AHI was higher in the COMISA ( $p = 0.01$ ), both groups expressed comparable daytime sleepiness ( $p = 0.16$ ). The COMISA group had no significant change in SF-36 and PSQI after 12 weeks of treatment and used CPAP much less frequently than OSA-only group ( $p = 0.001$ ).

**Conclusions** COMISA in Veterans with PTSD is associated with worse quality of life than those with OSA-only. Insomnia should be assessed in Veterans with PTSD who are not adherent to CPAP treatment.

**Keywords** Comorbid insomnia · Sleep apnea · Quality of life · CPAP · Adherence

## Introduction

In the last decade, several studies have documented a broad array of comorbid sleep disorders in subjects with PTSD

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This article is part of the Topical Collection on Comorbid Insomnia and OSA (COMISA) in Veterans

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including insomnia, nightmares, sleep-disordered breathing (SDB), and dream enactment behavior [1, 2]. Sleep impairment accounts for a significant portion of the variance in physical health complaints even after controlling for pain and depression [3]. In studies of active duty service members with PTSD who underwent polysomnography, 56.6 to 67.3% were diagnosed with obstructive sleep apnea (OSA) [4, 5]. This combination of OSA and PTSD results in worsened somnolence, fatigue, poor daytime function, and sleep-related quality of life compared with those with either condition alone and normal subjects [5]. Not infrequently, these same symptoms are experienced by Veterans suffering from insomnia, which makes the diagnosis and management of these cases quite challenging when both OSA and insomnia co-exist. In military personnel with combat exposure, comorbid insomnia and OSA, a condition originally termed “COMISA,” were identified in 38.2% of subjects presenting for initial evaluation of sleep disturbances [6].

The interaction between OSA and insomnia in Veterans with PTSD has not been fully elucidated. The conceptual

framework for the link between the two ailments conjectures a reciprocal relationship whereby each disorder amplifies the other. The disordered breathing events often result in transient arousals or complete awakening from sleep leading to difficulties in initiating and maintaining sleep. The somatic arousal experienced from recurrent apneic events may become conditioned to the bedroom producing a heightened state of arousal prior to sleep onset. PTSD acts as a catalyst promulgating maladaptive reinforcement. Due to sleep fragmentation of sleep apnea, interruption of memory consolidation contributes to resurgence of fear and anxiety [7]. As a result, a state of hyperarousal dominates sleep onset leading to chronic insomnia. The latter engenders sleep deprivation which adversely affects the tone of the pharyngeal muscles, particularly the genioglossus muscle, which in turn contributes to worsening of OSA increasing its severity [8].

The extent to which COMISA worsens PTSD or represents a by-product of PTSD remains ambiguous. Contemporary clinical studies of COMISA have provided informative data about incidence and risk factors, although most of those studies have emanated from cross-sectional studies or patients attending medical practices [9–13]. These characteristics varied as a function of the primary condition and were based on self-reported insomnia. More importantly, none of these studies have examined the influence of PTSD on the overall quality of life in the presence of these sleep comorbidities.

In this study, we aimed at exploring the health outcomes of Veterans with PTSD and COMISA before and following 12 weeks of CPAP treatment. We hypothesized that COMISA confers a worse quality of life and lower CPAP adherence in Veterans afflicted with PTSD and COMISA compared to a cohort of OSA-only Veterans.

## Methods

### Study population

Veterans with history of PTSD who presented to the sleep clinic at the VA Western New York Healthcare System (VAWNYHS) for management of sleep disorders between January 2014 and December 2016 were eligible to participate in the study. Inclusion criteria included the following: (1) diagnosis of PTSD established by a psychiatrist at least 6 months prior to the sleep clinic visit, (2) clinically stable with no change in psychotherapy regimen for at least 4 weeks before enrollment, (3) documented OSA by polysomnography, and (4) ability to provide an informed consent. Patients with mixed or central apnea, acute medical or psychiatric condition, or suicidal ideation were excluded from participation. Similarly, Veterans who were receiving opioids or who had prior CBT

treatment for insomnia were not eligible for enrollment. Some of these enrollees were part of a cohort group under study for the association between PTSD and obstructive sleep apnea [14]. The study was approved by the Institutional Review Board of VAWNYHS and all patients provided voluntary informed consent.

### Baseline assessment and follow-up visits

After obtaining informed consent, demographic, anthropomorphic, and socioeconomic characteristics were obtained from all participants, including include age, sex, body mass index (BMI), comorbidities, and medication list. Each patient was asked to complete the Epworth Sleepiness Scale (ESS) [15], the Insomnia Severity Index (ISI) [16], the PTSD checklist (PCL-M) [17], the Pittsburgh Sleep Quality Index (PSQI) [18], and the SF36 [19]. Subjects who scored greater than or equal to 15 points on the Insomnia Severity Index were categorized as having COMISA. An OSA-only group of Veterans with PTSD and OSA whose ISI score was < 15 was recruited simultaneously. Within 2 weeks of enrollment, a manual CPAP titration was performed according to standard criteria [20]. During CPAP setting, all participants received counseling on sleep hygiene using published materials to suggest ways to improve the regularity and duration of sleep, aiming for 7–8 h of sleep per night. Verbal and written directions on the use of CPAP were also provided, with instructions reinforced after the initial period of CPAP setup is completed, and then at interim telephone follow-up calls. A repeat assessment was conducted during a face-to-face visit scheduled 12 weeks following CPAP initiation.

### Assessment tools

**Epworth Sleepiness Scale** The ESS is a self-administered 8-item questionnaire used index to measure subjective sleepiness in OSA. Scores range from 0 to 24, with a cutoff of > 10 representing clinically significant sleepiness [15].

**Insomnia Severity Index** The ISI is a 7-item measure of perceived insomnia severity [16]. The ISI assesses sleep difficulties and distress, and impairment related to the sleep disturbance. Total scores range from 0 to 28, with a higher score indicative of greater insomnia severity. The ISI has excellent internal consistency (Cronbach  $\alpha = 0.74$ ) and temporal stability ( $r = 0.80$ ), has been validated with both sleep diary and polysomnography [16], and is sensitive to clinical treatment response [21]. Scoring guidelines consist of the following: score of 0–7 (no clinical insomnia), 8–14 (subthreshold insomnia), 15–21 (clinical insomnia of moderate severity), and 22–28 (severe insomnia).

**PTSD checklist** The 17-item PTSD checklist (PCL-M) is a validated self-report scale for assessing PTSD symptoms [17]. Items correspond to the DSM-IV symptoms of PTSD. Scores range from 17 to 85, with higher scores indicating more severe PTSD symptoms.

**SF-36** The SF-36 [19] is a generic 36-item Short-Form Medical Outcomes Survey (SF-36). It has eight main domains: physical functioning, role limitation due to physical problems, role limitation due to emotional problems, social functioning, mental health, energy/vitality, bodily pain, and general health perception. Each dimension item score is coded, summed, and transformed onto a scale from 0 to 100 (worst to best possible health). In addition, the 8 scales are used to form 2 distinct high-order summary scales: the physical component summary (PCS) and the mental component summary (MCS). The PCS includes the physical functioning, role physical, bodily pain, and general health scales, and the MCS includes the vitality, social functioning, role emotional, and general mental health scales. The raw scores for each subscale and the 2 summary measures are standardized, weighted, and scored according to specific algorithms.

**Pittsburgh Sleep Quality Index** The PSQI [18] is a self-rating questionnaire resulting in a global score between 0 and 21, which consists of seven dimensions of sleep quality. Since its introduction in 1989, the Pittsburgh Sleep Quality Index (PSQI) has gained widespread acceptance as a useful tool to measure sleep quality in different patient groups. Its good reliability and validity have been shown for patients with psychiatric and sleep disorders [22] and for patients with different somatic diseases [23]. The PSQI has internal consistency and a reliability coefficient (Cronbach's alpha) of 0.83 for its seven components.

### CPAP adherence

CPAP compliance was assessed at 12 weeks after initiation of therapy. Objective measures of CPAP use were obtained from a downloadable “smart card” compliance monitoring device. The percent of days used, the average time used per night for all nights, the average time used on nights CPAP worn, and the percentage of nights with  $\geq 4$  h of use were recorded. Similar to prior studies, adherence to CPAP was defined as the use of CPAP for  $\geq 4$  h per night on  $> 70\%$  of nights [24]. At the end of the study, participants answered two questions on a 7-point Likert scale indicating the extent of any discomfort/stress or interference in sleep that was a function of the CPAP.

### Statistical analysis

All analyses were performed with STATA software, version 13 (StataCorp, College Station, TX). Results for quantitative

variables were expressed as means  $\pm$  standard deviation. Data normality was assessed with the Shapiro-Wilk test. Discrete variables are summarized as frequency (group percentage). Proportions were compared using the Chi square test with Yates correction or Fisher's exact test when necessary. Continuous variables were compared using two-tailed *t* tests for variables with normally distributed data and Mann-Whitney rank sum test for non-normally distributed data. Spearman's rank correlation coefficients were used to assess the degree of association between two not normally distributed variables. A multivariate regression analysis to assess the association between the presence of COMISA and baseline MCS of SF-36, and PSQI after adjusting for severity of PTSD and AHI was performed. Subsequently, a multivariate logistic regression analysis was used to examine predictive factors of COMISA with those variables found to be contributory toward this outcome based on bivariate analysis. Only significant clinical and demographic variables from the initial group comparisons ( $p \leq 0.1$ ) were entered as confounders in the logistic regression analyses. A multicollinearity test was performed using the variance inflation factor to assess the degree of correlation between covariates. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). All tests are 2-tailed with a 0.05 significance level. The *p* value was corrected for multiple comparisons using the Bonferroni adjustment when indicated.

## Results

Baseline characteristics of the study population are shown in Table 1. Veterans with COMISA were younger and had lower BMI than those with OSA-only ( $p = 0.03$  and  $p < 0.001$ ; respectively). Female Veterans reported more frequently having insomnia in the presence of OSA than male Veterans did but the difference was not statistically significant ( $p = 0.15$ ). The prevalence of hypertension, chronic heart disease, and chronic pulmonary disease were similar in the two groups. However, depression was more common in Veterans with COMISA than those with OSA-only ( $p = 0.004$ ). Of the 49 patients in the entire sample receiving psychotropic medications, 63% were in the COMISA group and 37% in the OSA-only group ( $p = 0.001$ ). Overall, 5 patients with COMISA and one with OSA-only were receiving medications with sedating properties ( $p = 0.19$ ) [Fisher's exact test] (Table 1).

There was no difference between the two groups in excessive daytime sleepiness ( $p = 0.16$ ). The ISI score was  $26.0 \pm 6.4$  in the COMISA group versus  $11.8 \pm 2.3$  in the group of OSA alone ( $p < 0.001$ ). In Veterans with OSA who were experiencing insomnia, no significant correlation was noted between AHI and ISI ( $r = -0.07$ ,  $p = 0.64$ ). On polysomnography, the COMISA group experienced reduced total sleep time ( $p = 0.01$ ) and longer sleep latency ( $p < 0.001$ )

**Table 1** Patient characteristics

Variables	COMISA (n = 36)	OSA (n = 36)	p value
Age, years	47.2 ± 10.8	52.7 ± 9.7	0.03
Male sex, n (%)	26 (72)	31 (86)	0.15
BMI, kg/m <sup>2</sup>	31.4 ± 4.5	36.5 ± 6.9	<0.001
Hypertension, n (%)	17 (47)	22 (61)	0.24
Chronic heart disease, n (%)	4 (11)	6 (17)	0.49
Chronic pulmonary disease, n (%)	1 (3)	2 (6)	0.55
Depression, n (%)	26 (72)	14 (39)	0.004
Medications, n (%)			
Benzodiazepines	2	0	0.46
Non-benzodiazepine hypnotics	1	0	0.99
Sedative antidepressants	1	1	1.0
Sedating antihistamines	1	0	0.99
ESS	12.6 ± 4.2	13.9 ± 4.6	0.16
Polysomnography			
TST, h	5.4 ± 1.0	6.1 ± 0.72	0.01
Sleep efficiency, %	78.4 ± 15.7	79.1 ± 10.8	0.84
Sleep latency, h	0.73 ± 0.39	0.45 ± 0.57	<0.001
NREM (% of TST)	0.86 ± 0.3	0.88 ± 0.2	0.26
Diagnostic AHI, h <sup>-1</sup>	29.8 ± 18.3	40.7 ± 19.2	0.01
Arousal index, h <sup>-1</sup>	20.9 ± 12.4	34.3 ± 17.7	0.002
O <sub>2</sub> saturation nadir, %	85.7 ± 4.4	82.9 ± 6.4	0.14

than Veterans with OSA-only. However, there was no significant difference in the time spent in NREM sleep or nadir oxygen saturation between the two groups. AHI was significantly higher in Veterans with OSA than those with COMISA (AHI 40.7 ± 19.2 and 29.8 ± 18.3/h, respectively;  $p = 0.01$ ). By category, sleep apnea was more severe in the OSA-only group with 67% having AHI ≥ 30/h compared to 50% in the group with COMISA. In multivariate analysis, two factors—AHI and PCL-M—were included in the logistic regression after omitting age, depression, and BMI from the final model due to interrelatedness. Both AHI (OR 0.95; 95% CI 0.93–0.98,  $p = 0.01$ ) and PCL-M (OR 1.21; 95% CI 1.05–1.19,  $p < 0.001$ ) were highly predictive of COMISA in this population.

### CPAP response and adherence

Average CPAP pressure was not different between the COMISA group (9.0 ± 2.4 cm H<sub>2</sub>O) and OSA-only group (9.8 ± 2.2 cm H<sub>2</sub>O) ( $p = 0.13$ ). In both groups, the frequency of apnea and hypopnea events was reduced significantly following CPAP from 29.8 ± 18.3 to 4.2 ± 2.1/h in the COMISA group and from 40.7 ± 19.2 to 3.2 ± 2.6/h in the OSA-only group, respectively;  $p < 0.001$ ). However, Veterans with PTSD and COMISA demonstrated significantly lower CPAP adherence. Those with OSA alone used CPAP on 49.5% ± 32.6% of nights, for 3.5 ± 2.2 h/night. In comparison, patients

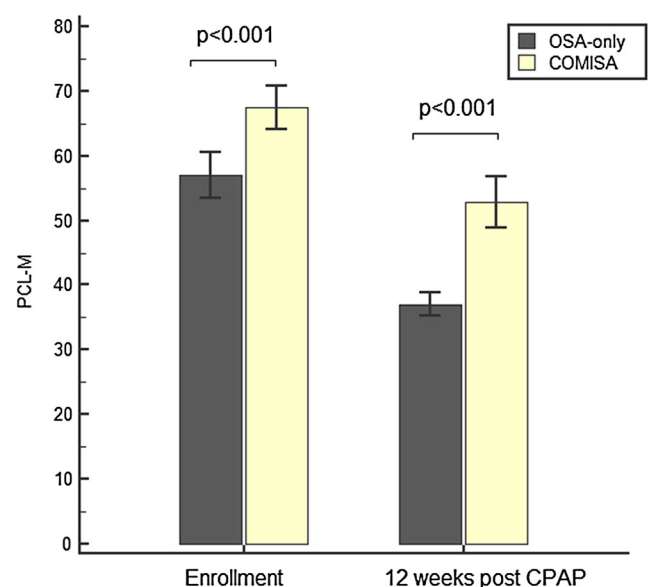
with PTSD and COMISA used CPAP on 32.9% ± 29.3% of nights ( $p = 0.001$ ), for an average of 2.2 ± 1.8 h/night ( $p = 0.03$ ). Resolution of sleepiness (ESS ≤ 10) occurred in 31.5% of PAP-adherent and 12.8% of PAP-non-adherent patients with COMISA, compared with 52.1% of PAP-adherent and 30.4% of non-adherent patients with PTSD and OSA-only. The ISI decreased in the COMISA group from 26.0 ± 5.9 at baseline to 24.8 ± 5.5 after CPAP but the difference did not attain statistical significance ( $p = 0.12$ ). Eight (22%) of the 36 patients with COMISA whom insomnia symptoms have abated had moderate to severe sleep apnea (AHI range 18–62). A positive correlation was observed between CPAP interference and onset of sleep (derived from PSQI) at 12 weeks follow-up visit ( $r = 0.48$ ,  $p = 0.03$ ).

### PTSD severity

At baseline, Veterans with COMISA exhibited worse PTSD symptomatology than those with OSA (67.5 ± 12.8 vs. 57.1 ± 10.3;  $p < 0.001$ ) (Fig. 1). Following CPAP treatment, the PTSD severity declined in both groups in comparison to baseline (67.5 ± 12.8 to 52.9 ± 11.8;  $p < 0.001$  in the COMISA group and 57.1 ± 10.3 to 37.0 ± 8.2;  $p < 0.001$  in the OSA-only group). However, the change in PCL-M between baseline and 12 weeks of CPAP was smaller in Veterans with COMISA than those with OSA-only (14.6 ± 11.3 vs. 20.1 ± 10.8;  $p = 0.03$ ).

### Sleep quality of life

Veterans with COMISA had a lower baseline MCS than those with OSA-only (35.5 ± 14.4 versus 46.1 ± 16.9;



**Fig. 1** Severity of PTSD in response to CPAP treatment

$p = 0.031$ ). Mental health, vitality, and role-emotional were the three domains of the SF-36 that had lower scores in the COMISA group in comparison to the OSA-only group. After eliminating age and BMI from the analysis due to multicollinearity, COMISA remained highly correlated with both the physical and mental component summary of SF-36 (Table 2). Only one domain-role emotional-showed an improvement in the COMISA group post-CPAP therapy (Table 3). However, the overall MCS was not different between baseline and week 12 of CPAP treatment ( $p = 0.27$ ). In contrast, the MCS for Veterans with OSA-only increased from  $46.1 \pm 16.9$  at baseline to  $61.8 \pm 19.6$  post-treatment ( $p < 0.001$ ). The improvement was observed in all four domains: mental health, vitality, social functioning, and role emotional. Interestingly, there was no improvement in the standardized physical component of SF-36 after treatment in either group.

At enrollment, PSQI results (Table 3) showed that perceived daytime dysfunction and sleep quality were significantly worse in the COMISA group compared to the OSA-only group ( $p = 0.008$  and  $p = 0.002$ ; respectively), as well as in the overall PSQI score ( $p = 0.003$ ). Perceived sleep efficiency, sleep duration, and sleep latency were comparable between the two groups at baseline. In multivariate analysis, COMISA was independently associated with baseline PSQI (Table 2). After 12 weeks of CPAP therapy, no significant changes were reported in any of the PSQI measures by Veterans with COMISA. However, there was a significant amelioration in the perceived sleep disturbances, sleep duration, and sleep latency in the OSA-only group after treatment. Similarly, the overall PSQI score decreased from  $10.2 \pm 1.8$  to  $7.8 \pm 2.5$  ( $p < 0.001$ ).

**Table 2** Association between COMISA and baseline PCS, MCS, and PSQI

Independent variables	Coefficient	Std. error	<i>t</i>	<i>p</i> value
<b>PCS</b>				
COMISA	24.38	3.57	6.82	<0.001
PCL-M	0.033	0.152	0.21	0.82
AHI	0.049	0.086	0.57	0.56
<b>MCS</b>				
COMISA	16.46	3.15	5.22	<0.001
PCL-M	0.36	0.13	2.70	0.008
AHI	0.051	0.076	0.67	0.50
<b>PSQI</b>				
COMISA	2.44	0.61	3.98	0.0002
PCL-M	0.019	0.026	0.75	0.45
AHI	0.012	0.014	0.81	0.42

COMISA comorbid insomnia and OSA, PCS physical component score, MCS mental component score, PSQI Pittsburgh Sleep Quality Index

## Discussion

In this case series of Veterans with PTSD, we have demonstrated that COMISA imparts greater morbidity than those experiencing a single disorder. Not surprisingly, COMISA was responsible for greater daytime impairment and worse quality of life than PTSD with OSA-only. Although treatment with CPAP remains the most effective therapy for OSA, the presence of concomitant insomnia appears to reduce adherence and lessens the benefits engendered by abolishing these respiratory events.

Evidence from prior clinical investigations in non-PTSD participants suggests that both OSA and insomnia co-exist with over half of the patients undergoing evaluation for OSA reporting at least one insomnia complaint [25, 26]. In Veterans with PTSD, the unusually erratic night-to-night changes in sleeping patterns as well as the nightmares-triggered fear of sleep add to the complexity of insomnia symptomatology. Currently, there is a dearth of epidemiologic studies on COMISA in civilians with PTSD. In one study involving 44 crime victims with nightmares and insomnia, almost half of participants had evidence of OSA [27]. To our knowledge, the prevalence of COMISA in Veterans with PTSD has not been determined. Given that OSA and insomnia are the two predominant sleep disorders in Veterans with PTSD, the causes and possible mechanisms of the reported association between OSA, insomnia, and PTSD require further evaluation in order to establish an effective therapy.

Data examining the relationship between severity of OSA and insomnia have been conflicting. While Yang and colleagues [28] denoted a lower probability of insomnia in patients with OSA, Gold and coworkers [29] found that AHI was positively correlated with the appearance of difficulty maintaining sleep in OSA; specifically, higher AHI corresponded to a greater probability of insomnia in patients with OSA. Yet Krakow et al. [30] reported that the appearance of insomnia in a group of patients with OSA was independent of AHI. In the current study, we observed no correlation between AHI and ISI in the COMISA group. However, a higher AHI predicted a lower likelihood of having COMISA. The conflicting observations among these studies suggest that the population profile, the methods used in establishing the presence of insomnia, and the myriad of underlying comorbid disorders such as depression and substance abuse should be accounted for in delineating the association between these disorders. Because these findings were observed in Veterans with PTSD, the interaction between insomnia and OSA may not be reproducible in other population. Hitherto, no study has assessed the temporal sequence of disease occurrence on the clinical manifestations of these two sleep disorders. It can be hypothesized that Veterans with OSA who acquire insomnia may have the capacity to overcome interruption in sleep pattern while Veterans with insomnia who develop OSA may

**Table 3** Subjective sleep quality of life before and after CPAP treatment

	COMISA		OSA	
	Pre	Post	Pre	Post
SF-36				
Mental health	46.0 ± 12.8	48.3 ± 16.7	60.1 ± 16.8*	74.8 ± 17.6†
Vitality	25.4 ± 15.3	27.7 ± 16.9	38.4 ± 18.9*	53.8 ± 22.9†
Physical functioning	40.5 ± 21.0	46.4 ± 19.7	59.3 ± 19.5*	62.8 ± 17.6
Social functioning	53.3 ± 19.4	57.1 ± 21.5	57.3 ± 22.7	72.0 ± 23.9†
Pain	50.6 ± 17.2	48.4 ± 17.3	54.0 ± 20.1	78.2 ± 18.2†
Role-physical	24.6 ± 10.5	24.8 ± 16.2	31.3 ± 23.6	37.5 ± 25.1
Role-emotional	17.2 ± 12.0	26.0 ± 13.6†	28.3 ± 14.7*	46.7 ± 14.1†
General health	40.6 ± 18.6	44.5 ± 21.6	45.0 ± 17.1	45.1 ± 19.5
PSQI				
Daytime dysfunction	2.0 ± 0.6	1.7 ± 0.5	1.3 ± 0.8*	1.2 ± 0.8
Sleep efficiency	1.7 ± 1.0	1.9 ± 1.2	2.0 ± 1.3	1.5 ± 1.0
Sleep disturbances	2.2 ± 0.4	1.8 ± 1.6	2.3 ± 0.4	1.7 ± 0.6†
Sleep duration	2.0 ± 0.9	1.6 ± 0.5	2.0 ± 0.7	1.1 ± 0.7†
Sleep latency	2.0 ± 0.6	1.7 ± 1.2	1.8 ± 0.6	1.0 ± 0.7†
Sleep quality	2.2 ± 0.7	1.8 ± 0.7	1.1 ± 0.4*	1.0 ± 0.5
PSQI	12.8 ± 3.4	11.7 ± 3.9	10.2 ± 1.8*	7.8 ± 2.5†

\*Indicates  $p < 0.05$  when comparing baseline COMISA to OSA alone

†Indicates  $p < 0.05$  when comparing pre- to post-CPAP treatment

have considerable reduction in sleep perception that any compensatory mechanism would be unable to adjust for sleep fragmentation. Whatever the mechanism involved or the order of disease occurrence, the co-existence of sleep apnea and insomnia is not uncommon, and the identification of these disorders is the first step in instituting a successful therapeutic management. Interestingly, we have observed no difference in the reported excessive daytime sleepiness between COMISA and OSA-only group. It is plausible that the sleep homeostatic pressure generated by the co-existence of insomnia and milder sleep apnea is displayed as excessive daytime sleepiness with similar intensity to those who have more severe OSA alone. We cannot dismiss the fact that underlying psychiatric disorders, more commonly observed in COMISA, may have amplified hypersomnia. Unless objective assessment of excessive daytime sleepiness is undertaken, a distinction between reported and actual excessive sleepiness would be difficult to ascertain.

Consistent with previous clinical studies [12, 13, 25, 28], we have observed that Veterans with PTSD and COMISA experience increased morbidity and reduced quality of life. The co-occurrence of insomnia with OSA imparts serious clinical implications on existing comorbidities that would be otherwise under control had these conditions been independently associated with either of these ailments. Previously, Smith and colleagues [10] reported that patients with OSA and comorbid insomnia experienced more symptoms of depression, anxiety, and stress than those with OSA. Similarly,

Krell and Kapur [25] reported a higher prevalence of psychiatric disorder in patients with OSA and comorbid insomnia than in patients with OSA alone. We found that all participants in our study population had PSQI total scores above the traditional cut-off score of 5, but the average scores were two points higher among those with PTSD and COMISA compared to those without indicating that both sleep quality and daytime functioning were severely deranged.

Given the significant decrease in PTSD severity following CPAP treatment [14], it was expected that the Veterans with COMISA would experience a reprieve from insomnia. Contrary to our expectations, insomnia severity did not change after OSA treatment. The poor adherence to CPAP in Veterans with COMISA may have curbed any benefits that may have resulted from suppression of apneic events. Contemporary investigations have found evidence for the negative impact of insomnia on CPAP use starting with the first 7 days of use and up to 2 years of follow-up. In a sleep clinic cohort of South Florida Hispanic veterans, the Insomnia Severity Index was the only independent predictor of 7 days CPAP use [31]. Another longitudinal study of 705 OSA individuals treated with positive airway pressure revealed that patients who reported symptoms of initial insomnia at baseline were more likely to be non-adherent at follow-up and this effect remained significant after adjusting for age, sex, BMI, smoking, and OSA severity [32]. Alternatively, the significant correlation between CPAP interference and sleep onset indicates that any improvement in insomnia that have occurred as

a result of OSA treatment may have been abrogated by the interference of the CPAP itself. We cannot exclude however that there may be a subgroup of patients that would experience relief from insomnia. Although we have not assessed the type of insomnia experienced by our participants, Bjornsdottir and coworkers [32] reported that patients who had frequent awakening at night were more likely to adhere to CPAP treatment while those who had difficulty falling asleep or going back to sleep after waking up early in the morning did not improve on CPAP treatment. In contrast, Wickwire and colleagues [33] have reported that difficulty maintaining sleep was consistently associated with less CPAP use as well as lower rates of adherence. Neither difficulty initiating sleep nor early morning awakening was associated with CPAP use. These observations have led to the belief that insomnia does not represent a symptom of sleep-disordered breathing but both insomnia and OSA represent distinct entities [34].

Despite the evidence-based proven treatments for insomnia disorder and OSA when they occur in isolation, treatment of COMISA and PTSD has not been widely studied, and few studies of treatment for COMISA in Veterans with PTSD have included sleep measures as outcomes [35, 36]. One study of VA providers treating Veterans with PTSD found that approximately 40% taught sleep hygiene techniques to PTSD patients with sleep problems [37]; however, prior studies and clinical guidelines suggest sleep hygiene education alone does not produce significant improvements in insomnia [38]. Recent research has demonstrated that use of behavioral sleep interventions can be effective as a means to reduce symptom severity and improve functional outcomes among individuals with PTSD and COMISA [39, 40]. Alternate models have used hypnotics with CPAP to overcome phobia and enhance adherence [41]. While none of our participants received any intervention for insomnia during the course of the study, available CBT modalities targeting COMISA in subjects with PTSD may only achieve a partial response. We conjecture that within the COMISA population there are different phenotypes depending on the presence of comorbid conditions, and type of insomnia with or without EDS [42]. Identifying these phenotypes would increase our ability to deliver a tailored adjunct therapy that can lead to sustainable CPAP treatment.

The current study has several limitations. First, the sample size was small and consisted primarily of Caucasian Veterans with PTSD. Given that the correlation between insomnia and OSA in PTSD remains scarce, whether such patterns are evident in other PTSD populations and geographical settings are not known. Second, because these data were derived from a clinical setting, the PTSD treatment delivered was tailored to individual needs and was not standardized. Third, despite the findings that Veterans with both insomnia and OSA had lower quality of life than those with OSA alone, a causality cannot be established, as we did not discern whether insomnia precipitated poor quality of life in patients with OSA or whether

poor quality of life was a risk factor for insomnia in OSA [43]. Fourth, the lack of a control group makes it difficult to determine whether the changes in PTSD severity and quality of life measures can be attributed to natural progression of the disease or CPAP treatment. However, the established efficacy of CPAP in improving symptoms of OSA poses an ethical challenge in performing randomized controlled trials in symptomatic patients with a control arm. Fifth, CPAP treatment in Veterans with COMISA showed less impact on quality of life measures compared to OSA-only Veterans following CPAP treatment. Although this blunted response suggests that the co-existence of insomnia with OSA may have been the culprit, it is plausible that the lower adherence to CPAP in COMISA patients would have yielded the same response. Due to the relatively low rate of CPAP adherence in our population, adjusting for average of CPAP use in a small sample limits interpretability of the results.

In conclusion, COMISA in the context of PTSD has a potentially detrimental effect on psychological health and overall well-being for Veterans. While recent military conflicts have drawn attention to the associations between poor sleep and health among military personnel, there remains limited research on the relationship between PTSD and COMISA, particularly among Veterans who are at higher risk for both sleep difficulties. Further research is needed to better identify risk factors for PTSD and COMISA and to develop and disseminate effective screening tools and treatments for this growing segment of the Veteran population.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the VA WNYHS institutional review board and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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