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Association of Psychiatric Disorders and Sleep Apnea in a Large Cohort

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Study Objectives: We conducted the present study to determine whether psychiatric disorders are commonly associated with sleep apnea in Veterans Health Administration beneficiaries.

Method: The Veterans Health Administration maintains several centralized databases containing healthcare data for more than 4 million veterans. We reviewed data from 1998 to 2001 and identified patient records having International Classification of Diseases-Ninth Edition-Clinical Modification codes indicating sleep apnea and various psychiatric conditions. Subsequently, we compared age, sex, ethnicity, and prevalence of comorbid psychiatric conditions for Veterans Health Administration beneficiaries with and without sleep apnea.

Results: Out of 4,060,504 unique cases, 118,105 were identified as having sleep apnea (estimated prevalence of 2.91%). Mean age at the time of diagnosis was 57.6 years. Psychiatric comorbid diagnoses in the sleep apnea group included depression (21.8%), anxiety (16.7%), posttraumatic stress disorder (11.9%), psychosis (5.1), and bipolar disorders (3.3%). Compared with patients not diagnosed with sleep apnea, a significantly greater prevalence ($P < .0001$) was found for mood disorders, anxiety, posttraumatic stress disorder, psychosis, and dementia in patients with sleep apnea.

Conclusions: Sleep apnea is associated with a higher prevalence of psychiatric comorbid conditions in Veterans Health Administration beneficiaries. This association suggests that patients with psychiatric disorders and coincident symptoms suggesting sleep-disordered breathing should be evaluated for sleep apnea.

Keywords: Sleep apnea/hypopnea syndrome, depression, psychosis, posttraumatic stress disorder (PTSD), anxiety, bipolar disorder

Citation: Sharafkhaneh A; Giray N; Richardson P et al. Association of psychiatric disorders and sleep apnea in a large cohort. *SLEEP* 2005;28(11): 1405-1411.

INTRODUCTION

SYMPTOMATIC OBSTRUCTIVE SLEEP APNEA (OSA) AFFLICTS AN ESTIMATED 4% OF MEN AND 2% OF WOMEN AGED 30 TO 70 YEARS IN THE UNITED States.[1] OSA is characterized by repeated pharyngeal obstructions during sleep, causing airflow cessation (apnea) or reduction (hypopnea). Respiratory events produce arousals, fragment sleep, and are often accompanied by oxygen desaturations. Common symptoms include daytime sleepiness, fatigue, irritability, disturbed sleep, memory problems, and diminished quality of life.[2,3] In addition to cardiovascular disorders and other medical conditions, recent epidemiologic studies link untreated OSA to multiple psychiatric conditions, including depression and anxiety.[4]

Investigators have long explored and debated a possible link between psychiatric disorders and sleep apnea. Although some studies failed to show a significant correlation between psychiatric disorders and sleep apnea, most revealed a significant association between the psychiatric disorders (specifically depression) and sleep apnea.[3, 5-7] The mechanisms underlying such a relationship are not fully elucidated. The mood disturbance may represent a biologic and/or psychosocial consequence of sleep apnea. Conversely, psychiatric disorders may contribute to and promote development of sleep disturbances. Still other researchers suggest that both conditions relate to common underlying mechanisms. It has been suggested that hypoxemia, and to some extent sleep fragmentation, may provoke depressive symptoms.[8] It is also possible that depressed mood may simply result from any chronic medical conditions, including sleep apnea.[9] Regardless of how sleep apnea is linked to depressed mood, growing evidence indicates that patients with OSA have impaired quality of life and impaired neurocognitive functioning.[3,10]

The United States Veterans Health Administration (VHA) provides health care to more than 4 million veterans. In 1970, VHA began developing centralized databases to monitor the care provided and store related information for each inpatient or outpatient visit. Recently, investigators from Michael E. DeBakey VA Medical Center's Health Services Research and Development used these databases to determine hospital use and survival among VHA beneficiaries.[11] In a survey of VHA beneficiaries in 1999, point prevalences for psychiatric disorders were reported: 15.1% for depression, 8.8% for anxiety, 6.8% for PTSD, 11% for alcohol abuse, 4.6% for schizophrenia, and 4% for bipolar disorders.[12] The prevalence of these disorders stratified by the presence or absence of a sleep apnea diagnosis is not known. The purpose of the present study was to systematically assess whether sleep apnea confers any additional risk for psychiatric disorders among VHA beneficiaries.

METHOD

This is a retrospective, cross-sectional, database review of all VHA outpatient clinic file or patient treatment file records be-

Disclosure Statement

This was not an industry supported study. Dr. Hirshkowitz has received research support from Sanofi, Merck, Neurocrine, Takeda, Lundbeck, Orphan, Aventis, Somaxin, Sepracor, and Cephalon; and is a member of the speaker bureau for Sanofi, Takeda, Sepracor, and Cephalon. Dr. Young has participated in speaking engagements supported by Sanofi-Synthelabo, Scripps, ResMed, and Cephalon; and is a member of the Advisory Board for Pfizer and SMEI. Drs. Sharafkhaneh, Giray, and Richardson have indicated no financial conflicts of interest.

Submitted for publication November 2004
Accepted for publication July 2005

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Table 1—ICD-9 CM and CPT codes

Disease	Codes	Description
Chronic medical conditions	401-404	Hypertension
	412-414	Cardiovascular disease
	428	CHF
	430-437	Cerebrovascular accident
	278.0	Obesity
	250.0	Diabetes
	490-492, 496	COPD
Depression	296.2	Major depression single episode
	296.3	Major depression recurrent episode.
	296.9	Other and unspecified affective psychosis
	311	Depressive disorder NOS
Anxiety	300	Neurotic (anxiety) disorder, NOS
	308	Acute reaction to stress
	309	Adjustment reaction
	306	Physiological malfunction arising from mental factors
PTSD	309.81	Post traumatic stress disorder
Alcohol dependency	291	Alcohol induced mood disorder
	303	Alcohol dependence
	305	Alcohol abuse
Psychosis	295	Schizophrenic disorders
	297	Delusional disorders
	298	Other non-organic psychosis
Bipolar Disorders	296.1	Manic disorder-recurrent episode
	296.4-296.8	Bipolar affective disorders
Substance abuse	292	Drug psychosis
	304	Drug dependence
	305.2-305.7	Specific drug abuse
	305.9	Other/unspecified drug abuse
Dementia	290	Senile and pre-senile organic psychotic conditions
	293	Transient organic psychotic conditions
	294	Other organic psychotic conditions (chronic)
	310	Specific non-psychotic mental disorders due to organic brain damage

ICD-9-CM refers to International Classification of Diseases-Ninth Edition-Clinical Modification; CPT, current procedural terminology code; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; PTSD, posttraumatic stress disorder; NOS, not otherwise specified.

tween the beginning of fiscal year 1998 to the end of fiscal year 2001. This study was approved by the local institutional review board and R&D committee.

Databases

The Patient Treatment File

During the study period (1998-2001), each annual main file of the patient treatment file contained approximately 500,000 hospitalization records among more than 300,000 United States military veterans. The patient treatment file was first established in 1970, and it registers all hospitalizations from 172 VHA hospitals throughout the United States. Trained coders enter diagnoses recorded by practitioners at each VHA facility into the local computer system (VISTA). This information is then automatically transferred to the central VHA database in Austin, Texas. Each hospitalization has a primary discharge diagnosis and up to 9 secondary diagnoses. Medical diagnoses have been encoded according to the ninth revision of the Clinical Modification of the International Classification of Diseases [ICD-9-CM].

The Outpatient File

In 1997, VHA began recording diagnoses made during each outpatient encounter in the outpatient file. Using a unique identifier (social security number), an individual can be tracked through the different files of the patient treatment file and the outpatient file to obtain a complete record of encounters in the system.

Procedure

We searched the VHA's inpatient hospitalization (patient treatment file) and outpatient clinic visit databases for ICD-9-CM diagnostic codes. For sleep apnea, these codes include: (1) insomnia with diagnosed sleep apnea (780.51), (2) hypersomnia with diagnosed sleep apnea (780.53), and (3) other unspecified diagnosed sleep apnea (780.57). A total of 122,054 patients were identified in fiscal years 1992 through 2001 databases (1992-2001 in the patient treatment file and 1997-2001 in the outpatient file). A sample of 118,105 patients was constructed using the following 2 criteria: (1) the patient's first coded instance for sleep apnea occurred between October 1, 1998 through September 30, 2001 (inclusive) and (2) the patient's age at first occurrence was between 21 and 85 years.

Collected Information

Variables were extracted and tabulated for patients with sleep apnea and for the parent population without sleep apnea. In addition to demographic variables (sex and ethnicity), ICD-9-CM codes for comorbid psychiatric conditions were tabulated (Table 1), including (1) psychotic disorders, (2) depressive disorders, (3) posttraumatic stress disorder (PTSD), (4) bipolar disorders, (5) anxiety disorders, (6) dementia/delirium, (7) alcohol dependence, and (8) drug use (other than alcohol). All fourth and fifth digits of the ICD-9-CM codes were used unless otherwise specified. These categories were created by 1 of the authors, who is a board-certified psychiatrist (NG). Only ICD-9-CM codes that are indicative of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition axis I disorders (clinical disorders) were included. We did not consider axis II personality disorders, sexual disorders, developmental disorders and mental retardation, conduct and impulse control, and V code (social problems).

To differentiate effect of other chronic conditions on prevalence of psychiatric disorders, we used ICD-9-CM codes for chronic medical conditions (Table 1) to separate sleep apnea subjects with and without chronic medical conditions. Subsequently, we compared psychiatric comorbid prevalence between these 2 groups.

SAS v8.2 (SAS, Inc., Cary, NC) was used to extract demographic variables and diagnosis history (ICD-9-CM codes), to construct datasets suitable for our analyses on the basis of these extracts, and for data analysis. Patient records were selected by scrambled social security numbers, and the records in the analysis datasets were then de-identified by way of assignment of unique study identifier that could not be decoded to the patient's social security number.

Table 2—Demographic Characteristics of Patients in the Apnea Group and Parent Population (the Non-apnea Group)

Characteristics	Apnea Group	Non-apnea Group	P value
Number	122,052	3,525,276	
Mean age, y (SD)	57.6 (12.47)	59.03 (15.58)	< .0001
Men	96	90	< .0001
Age distribution, y			
< 34	7.22	4.24	< .0001
35-64	49.99	57.37	< .0001
> 65	42.79	38.4	< .0001
Ethnicity			
White	40.5	59	< .0001
Black	9.6	11	< .0001
Hispanic	3.5	4	> .05
Unknown	45.75	26	<0.0001
Medical comorbidities			
HTN	60.1	39.2	< .0001
Obesity	30.5	6.8	< .0001
Diabetes	32.9	16.3	< .0001
HF	13.5	4.4	< .0001
CVD	27.6	16.8	< .0001
CVA	5.7	3.7	< .0001
COPD	6.8	2.7	< .0001

Data are presented as percentages unless otherwise noted. HTN refers to hypertension; HF, heart failure; CVD, cardiovascular disease; CVA, cerebrovascular accident; COPD, chronic obstructive pulmonary disease.

Table 3—Psychiatric Conditions in the Apnea Group and Parent Population (Non-apnea Group)*

Psychiatric Conditions	Apnea Group	Non-apnea Group	Odds Ratio (95% CI)	χ^2 P value
Number	122,052	3,525,276		
Depression	21.75%	9.43%	2.67	<.0001
	26,551	332,266	(2.63-2.71)	
Anxiety	16.67%	8.39%	2.18	<.0001
	20,344	295,716	(2.15-2.22)	
PTSD	11.85%	4.74%	2.70	<.0001
	14,459	16,727	(2.65-2.74)	
Alcohol	5.53%	5.68%	0.97	0.027
dependence	6,745	200,065	(0.95-0.99)	
Psychosis	5.13%	3.75%	1.40	<.0001
	6,260	132,111	(1.35-1.43)	
Bipolar	4.06%	1.88%	2.20	<.0001
disorders	4,950	66,412	(2.15-2.27)	
Substance	3.32%	3.28%	1.01	0.4095
abuse	4,056	115,643	(0.98-1.05)	
Dementia	2.13%	1.81%	1.18	<.0001
	2,596	63,732	(1.13-1.23)	

In the statistical analysis, age, sex, and ethnicity were entered as controlling covariates. CI refers to confidence interval; PTSD, post-traumatic stress disorder.

Data Analysis

The demographic variables in the analysis dataset included age, sex, and ethnicity. Comorbid condition variables were defined on the basis of occurrence of the ICD-9-CM diagnostic codes.

Mean, SD, and frequency distribution by age, ethnicity, sex, and diagnostic codes were calculated. Inferential analysis comparing patient with sleep apnea to the parent population was conducted. Comorbid ICD-9-CM codes were tabulated from clinic visits during fiscal year 2000 and hospital stays with discharge dates that fell within 2000. Two-sided 95% confidence intervals (CI) for unadjusted odds ratios and P values for χ^2 test statistics were calculated to compare the comorbidity rates for patients with and without sleep apnea. Odds ratios adjusted for demographic variables were also estimated by multivariate logistic regression, with the comorbid conditions as outcomes, sleep apnea as explanatory variable, and age, sex, and ethnicity as controlling covariates. Comparisons were performed by calculating P values for χ^2, Student t tests, and Wilcoxon test statistics.

RESULTS

Table 2 shows demographics for patients with sleep apnea (apnea group) and for patients not diagnosed with sleep apnea (non-apnea group). Mean age at diagnosis was 57.6 years (SD ± 12.47), with 38.4% older than 65 years of age. The majority of patients with diagnosed sleep apnea were age 35 to 64 years. Detailed results related to prevalence of diagnosed sleep apnea among VHA beneficiaries have been reported previously.[13]

Table 3 presents the prevalence of psychiatric comorbid conditions in the apnea group and the non-apnea group. Depressive disorders (21.75%), anxiety disorders (16.67%), PTSD (11.85%), psychotic disorders (5.13), bipolar disorder (4.06%), and dementia (2.13%) were statistically significantly more prevalent in the apnea group compared with the non-apnea group.

Table 4 shows data and the prevalence of comorbid psychiatric conditions for subjects with a sleep apnea diagnosis in year 2000 actively using VHA (apnea group) and non-apnea group (with active VHA file in year 2000) who were not diagnosed as having any other chronic medical conditions. The differences between groups remain significant for most psychiatric conditions studied.

We compared the prevalence of sleep-apnea diagnoses in subjects with and without specific psychiatric diagnoses. Sleep apnea diagnoses were significantly more common in subjects with depression compared with those without depression (3% vs 1%, with an odds ratio of 2.7 and 95% CI of 2.27 and 3.10), anxiety (2% vs 1% with an odds ratio of 2.3 and 95% CI of 2.08 to 2.41), PTSD (3% vs 1% with an odds ratio of 2.98 and 95% CI of 2.1 to 3.6), psychosis (2% vs 1% with an odds ratio of 1.35 and 95% confidence interval of 1.05 to 1.69), bipolar disorders (3% vs 1% with an odds ratio of 2.32 and 95% CI of 2.02 and 2.63), and dementia (2% vs 1% with an odds ratio of 1.49 and 95% CI of 1.05 and 1.92).

Table 5 compares the prevalence of comorbid psychiatric conditions among patients with the different sleep apnea ICD-9-CM codes. Regardless of the diagnostic category, the prevalence of a comorbid condition was systematically higher in patients with OSA compared with the Non-apnea group.

DISCUSSION

Our data show that the prevalence for comorbid psychiatric conditions is significantly higher in individuals with diagnosed sleep apnea than in individuals not diagnosed with sleep apnea. This pattern was most pronounced for mood disorders (depression and bipolar disorder), PTSD, and other anxiety disorders. The prevalence of these psychiatric conditions remained high in

Table 4—Psychiatric Comorbidities in the Apnea Group and the Parent Population (Non-apnea Group) Without any Other Medical Comorbidity During Year 2000

Comorbidity	Apnea Group	Non-apnea Group	Odds Ratio (95% CI)	χ^2 P value
Number	20,492	16,814,85		
Depression	19.66%	8.27%	2.71	< .0001
	4,028	139,072	(2.62-2.81)	
Anxiety	15.54%	7.4%	2.3	< .0001
	3,185	124,417	(2.22-2.39)	
PTSD	12.86%	4.71%	2.98	< .0001
	2,636	79,279	(2.86-3.11)	
Alcohol	6.05%	6.09%	0.99	> .8
Dependence	1,239	102,379	(0.94-1.05)	
Psychosis	5.08%	3.81%	1.35	< .0001
	1,040	64,054	(1.27-1.44)	
Bipolar	4.65%	2.06%	2.32	< .0001
disorders	953	34,600	(2.17-2.48)	
Substance	4.26%	4.15%	1.03	> .415
abuse	873	69,715	(0.96-1.10)	
Dementia	1.6%	1.1%	1.50	< .0001
	327	18,020	(1.34-1.67)	

In the statistical analysis age, sex, and ethnicity were entered as controlling covariates. The medical comorbidities excluded are those listed in Table 2, including hypertension, heart failure, cardiovascular disease, cerebrovascular accident, and chronic obstructive pulmonary disease. CI refers to confidence interval; PTSD, posttraumatic stress disorder.

Table 5—Prevalence of Psychiatric Comorbid Conditions by ICD-9 Classifications for Sleep Apnea in 92,653 Patients

ICD-9 Code	780.51	780.53	780.57	Multiple	P value
Subjects, no.	6824	16961	67903	965	
Frequency	6.91	17.17	68.73	0.98	
Depression	17.65	15.67	14.27	15.06	< .0001
Anxiety	17.89	14.99	12.39	14.29	< .0001
PTSD	7.6	7.2	6.0	6.2	< .0001
Alcohol dependence	6.57	4.99	4.66	4.28	< .0001
Psychosis	5.05	3.93	3.20	4.18	< .0001
Bipolar	3.94	3.24	2.70	3.50	< .0001
Substance abuse	4.90	3.76	2.89	4.37	< .0001
Dementia	2.25	2.08	1.84	1.46	.0134

Data are presented as percentages unless otherwise specified. ICD-9 refers to International Classification of Diseases, ninth edition; PTSD, posttraumatic stress disorder.

patients with sleep apnea even when controlling for other chronic medical conditions.

The association between depression and OSA remains controversial. Nonetheless, results using this very large population indicate that more than 21% of veterans with sleep apnea had comorbid depression. These data are consistent with the results of multiple smaller studies.[6, 14-16] Interestingly, our findings are very similar to a report by Reynolds and coworkers that 20% of patients with OSA met criteria for a past or present episode of depression.[6] By contrast, some other studies have not found an increased prevalence of depression in patients with OSA. A 5-year longitudinal study of older adults with mild OSA did not show a significant psychopathology.[17] Similarly Pillar [18] and colleagues, in a study of 2,271 individuals using a symptom self-report inventory (SCL-90), failed to find a link between the existence or severity of OSA with depression. Contrary to Pillar's finding, Yue and colleagues,[19] using the same instrument, found elevated somatization, obsession-compulsion, depression, anxiety, and hostility in patients with sleep apnea compared with normal subjects. Our data also show that subjects with depression compared with nondepressed controls have a higher prevalence of sleep apnea diagnoses (7.4% vs 2.9%). Although causality cannot be discerned from these data, intervention studies provide important clues. Means and colleagues[20] showed that treatment of OSA with continuous positive airway pressure (CPAP) reduced the depressive symptoms. Furthermore, a systematic review of randomized trials of CPAP therapy in OSA have shown improved mood after treatment.[22]

From a psychiatric perspective, one can conceptualize the relationship between depression and sleep apnea using several models: (1) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, describes a type of depressed mood that is a direct physiologic consequence of a general medical condition[21] and (2) hypoxemia, and to some extent sleep fragmentation, reportedly can cause depressive symptoms.[8] By this definition, depression related to sleep apnea would be considered as a depression secondary to a general medical condition.[22] In contrast, excessive daytime sleepiness and fatigue resulting from sleep apnea can lead to significant social and personal problems and result in depression.[9] Regardless of the nature of the relationship between the 2 conditions, in our large sample, the veterans with sleep apnea had higher rates of depression than the control group of veterans who carry the same risk factors for other medical comorbidities.

Depression is associated and may manifest as insomnia. Furthermore, a patient diagnosed with sleep apnea who also complains of insomnia may have a greater probability of also being diagnosed with depression. Therefore, it is also likely that the association of OSA and depression relates to the presence of insomnia as a confounding factor. However, when we examined the separate diagnostic codes for sleep apnea, we found that the prevalence of depression was higher in patients with sleep apnea compared with subjects without apnea, regardless of the presence or absence of insomnia.

Sleep apnea and depression can be bridged conceptually by vital exhaustion. Vital exhaustion refers to a state characterized by elevated somatic and cognitive symptoms of depression without affective symptoms. Van Diest and colleagues[23] formalized a vital exhaustion scale using elements of the Beck Depression Inventory. The authors studied a cohort of cardiac patients and reported that the vital exhaustion without "depressed mood" is the major manifestation of depression. In a similar study, we found Beck Depression Inventory elevations consistent with vital exhaustion profiles in patients with sleep apnea.[24] Millmann and colleagues,[5] using the Zung depression scale, identified a depression profile in patients with sleep apnea that was similar to vital exhaustion as described by Van Diest. Therefore, depressive manifestations in patients with sleep apnea may reflect the patients' vital exhaustion and would differ dramatically from melancholic affective mood changes observed in more typical forms of depression and dysthymia. As such, depressive phenomenon in patients with sleep apnea should be more akin to depression secondary to chronic medical illness.

The association between OSA and anxiety has also been recorded. Data from the present study support a strong association between diagnosed sleep apnea and anxiety. The prevalence of sleep apnea in patients with anxiety is significantly higher than in subjects without anxiety (2.5% vs 1.1%). Yue et al[19] reported that patients with OSA have higher anxiety scores than controls (measured by General Severity Index). Further evidence points to a relationship between nocturnal panic attacks and OSA.[25,26] Similarly, Borak and colleague[27] reported a strong correlation between anxiety and apnea-hypopnea index.

Sleep problems are cardinal symptoms of PTSD, and the relationship between PTSD and OSA has been a subject of recent interest. Our data strongly support an association between sleep apnea and PTSD. Similarly, Krakow and colleagues[28-30] reported a highly increased prevalence of comorbid behavioral and medical sleep disorders in trauma patients. The same authors have suggested an arousal-based mechanism initiated by posttraumatic stress-promoting OSA development in a trauma survivor.[30] Interestingly, in a case series and a case report, CPAP treatment of OSA improved insomnia, nightmares, and PTSD symptoms.[28,31] By contrast, Klein[32] reported no evidence of sleep disturbance when comparing a small sample of trauma patients with and without PTSD.

Our data show that psychosis is significantly more common in subjects with diagnosed sleep apnea compared with patients not diagnosed with sleep apnea. Additionally, the prevalence of sleep apnea was slightly higher in patients with psychosis compared with patients who were not psychotic (1.6% vs 1.2%). This finding is consistent with the literature. Fifteen percent of patients with schizophrenia screened in a sleep clinic had sleep-disordered breathing.[33] Ancoli-Israel and colleagues,[34] using a respiratory disturbance index of 10 or greater as the definition of sleep apnea, reported an even higher prevalence (48%) in patients with schizophrenia. Furthermore, case reports indicate that treating sleep apnea may improve psychotic symptoms.[9]

An association between sleep apnea and substance and alcohol abuse has been reported;[35-40] however, we did not find an increased prevalence of substance abuse in the apnea group (3.32%) compared with the non-apnea group (3.28%). The prevalence for alcohol dependence in VHA beneficiaries is reportedly high (11%);[12] however, in our study, the prevalence was only 5.68% in the general VHA population and 5.53% in subjects with sleep-apnea diagnoses. In general psychiatric settings, 20% to 50 % of men and 6% to 10% of women suffer from alcoholism.[41] Considering that only 20% to 50% of alcoholic patients in a general practice are recognized and diagnosed,[41] a prevalence of 5.68% in our database is consistent. Using Table 3, the estimated prevalence of sleep apnea in alcoholic and nonalcoholic subjects is similar (3.3% and 3.5%, respectively). By contrast, Aldrich and colleagues[34] described an age-dependent increase in the prevalence of polysomnographically diagnosed sleep apnea in their cohort of abstinent alcoholics. Our reliance on a retrospective database and ICD-9-CM diagnostic codes in this study may explain some of the difference between our results and those of others. In this study, sleep apnea is a clinical diagnosis. Other studies reporting an association of sleep apnea and alcohol abuse use polysomnography as the diagnostic criterion for sleep apnea. Furthermore, alcohol-abuse diagnoses in our study are based on healthcare providers' report. We did not use any specific screening tools to confirm or expand the diagnosis. Therefore, the lower prevalence in our study can be due to selection and assignment biases. In addition, several methodologic issues make comparing prevalence data in 2 chronic conditions difficult. These issues include diagnostic methods used, differentiation between ongoing versus past history of alcohol use, and the definition of sleep apnea.

Our data show a higher prevalence of dementia in subjects with OSA compared with the rest of VHA population. Strong associations between OSA and cognitive function (eg, impaired reaction-time, memory, and executive function) are well documented.[42-44] The prevalence of sleep apnea is higher in patients with Alzheimer disease compared with elderly controls.[45,46] However, other studies have failed to show this association.[47,48] Previous work has used small samples of elderly subjects with dementia and were likely underpowered. Furthermore, the association between sleep apnea and dementia is influenced by the etiology of dementia. Patients with vascular dementia have a higher incidence of OSA compared with patients with Alzheimer dementia.[49]

In the present study we examined a centralized administrative databases. We did not validate cases by examining the patients' written medical record. The accuracy of diagnoses in VHA administrative databases has been studied by comparing data from these databases with written medical records. In such a study, Szeto and colleagues[50] concluded that the administrative database across several visits is accurate and efficient at determining chronic medical diagnoses.

Nevertheless, there are a variety of limitations associated with this research methodology, perhaps the most important being variable precision and technique with which diagnoses are confirmed. The study does suffer from a major weakness that these databases probably have inconsistent ascertainment. Some VHA programs rely on cardiopulmonary or overnight oximetry; therefore, underdiagnosing sleep apnea using nonpolysomnographic techniques is more likely than when comprehensive laboratory polysomnography is used.[51,52] By contrast, overestimation of sleep-apnea prevalence by physician diagnoses has also been reported.[53]

Other sources of error include coding inaccuracies and variance across multiple sites and coders. In 2002, there were 163 hospitals and 913 outpatient clinics providing health services. Our search related to the incidence of sleep-apnea diagnoses across different VHA centers did not show significant heterogeneity. However, there is no reason to believe that systematic miscoding occurred in the sleep-apnea group compared with the parent population. Another concern is database integrity and continuity when data codes are altered or updated. To our knowledge, there has not been any significant coding change across the years of data entry. ICD-9-CM codes have been stable and unambiguous for sleep apnea and the comorbid conditions we analyzed. Databases are notorious for having repeat entries; therefore, we checked and only accepted 1 data record per social security number.

Perhaps the greatest limitation of our data relates to sampling bias. Our epidemiologic measurement is limited to the veterans who use the VHA system. Our prevalence figures may be underestimates to the extent that we could not capture our cohort members' use of non-VHA services. Generally, veterans who use the VHA system are more likely to be middle aged or older men and often have multiple comorbid conditions. Therefore, care must be taken when attempting to generalize our results to the general population. However, with respect to comorbid psychiatric conditions, the sampling bias is equivalent for groups with or

without comorbid psychiatric conditions, unless one thinks there is a differentially greater propensity to order sleep assessments on psychiatric patients. For such a bias to operate, the overall prevalence of sleep-disordered breathing would have to be much higher (which is likely); however, one would also expect all psychiatric diagnostic groups to approach the elevated prevalence (which they do not). Furthermore, in our experience, more sleep evaluations are ordered by primary care, otorhinolaryngology, and medicine than psychiatry. Thus, whatever population bias exists, it is not likely confounded with our groupings. Nonetheless, even with potential sampling bias, knowing the prevalence of sleep apnea and its association with psychiatric comorbidities within VHA beneficiaries is important information, potentially useful for resource allocation. Although the current study shows significant associations, because of the cross-sectional nature of our study, we were not able to determine the temporality of the associations. In summary, psychiatric comorbid conditions, especially mood disorders, anxiety disorders, and dementia, are common in VHA beneficiaries with sleep apnea. Further studies are needed to establish the true prevalence of these conditions in patients with sleep apnea. Accurate information is required for appropriate resource allocation to meet the healthcare needs of VHA beneficiaries. In addition, it is not clear to what extent treatment would improve these comorbid conditions. The results of therapeutic interventions for these patients in terms of healthcare utilization and cost remain to be determined.

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