Obstructive Sleep Apnea and Pain Intensity in Young Adults

Wardah Athar¹, Mary E. Card², Antonios Charokopos³, Kathleen M. Akgün^{1,4}, Eric C. DeRycke⁴, Sally G. Haskell^{1,4}, Henry K. Yaggi¹, and Lori A. Bastian^{1,4}

¹Yale University School of Medicine, New Haven, Connecticut; ²Division of Pulmonary and Critical Care Medicine, Johns Hopkins University, Baltimore, Maryland; ³Division of Pulmonary, Critical Care and Sleep Medicine, Icahn School of Medicine at Mount Sinai, New York, New York; and ⁴Pain Research, Informatics, Multimorbidities, and Education Center, Veterans Affairs Connecticut Healthcare System, West Haven, Connecticut

Abstract

Rationale: Prior research studies on the association of obstructive sleep apnea (OSA) and pain intensity have examined older patients; there is a need to understand the relationship between OSA and pain intensity among younger adults.

Objectives: To examine whether young adults with diagnosed OSA are more likely to report higher pain intensity compared with those without OSA.

Methods: We conducted a cross-sectional analysis of a cohort study of Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn veterans who had at least one visit to a Veterans Health Administration primary care clinic between 2001 and 2014. OSA was identified using one inpatient or two outpatient *International Classification of Diseases, Ninth Revision* codes from electronic medical records. Average pain intensity (based on the self-reported 0–10 numeric rating scale over a 12-month period) was categorized as no pain/mild (0–3; no pain) and moderate/severe (4–10; significant pain). Covariates included

age, sex, education, race, mental health diagnoses, headache diagnoses, pain diagnoses, hypertension, diabetes, body mass index, and smoking status. Multivariate logistic regression models were used, and multiple imputation was performed to generate values for missing variables.

Results: We identified 858,226 young adults (mean age 30 yr [SD = 7]), of whom 91,244 (10.6%) had a diagnosis of OSA and 238,587 (27.8%) reported moderate/severe pain for the 12-month average. With young adults without OSA, those with OSA were more likely to report moderate/severe pain intensity (adjusted odds ratio, 1.09; 95% confidence interval, 1.08–1.11) even after controlling for covariates.

Conclusions: We found that young adults with OSA have greater odds of comorbid moderate/severe pain. Because of the high prevalence of chronic pain in younger adults, this study highlights the need to understand the impact of OSA diagnosis and treatment on pain intensity. Future work is needed to determine the role of effective OSA treatment on pain intensity over time in these young adults.

Keywords: sleep apnea; veterans; pain intensity; headache

(Received in original form October 14, 2019; accepted in final form July 9, 2020)

Supported by the Office of Research and Development and Health Services Research and Development in the Department of Veterans Affairs of the Veterans Health Administration (IIR 12-118 and CIN 13-407), the Yale School of Medicine Medical Student Fellowship, and the U.S. National Institutes of Health (award T35HL007649).

Author Contributions: W.A. and L.A.B. contributed to the study design, data analysis, data interpretation, and drafting/revising the work. E.C.D. contributed to the study design, data acquisition, data analysis, data interpretation, and revising the work. M.E.C., A.C., K.M.A., S.G.H., and H.K.Y. contributed to the study design, data interpretation, and drafting/revising the work. All authors approved the final version of the work and agree to be accountable for its accuracy and integrity. The views expressed in this manuscript are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government.

Correspondence and requests for reprints should be addressed to Lori A. Bastian, M.D., M.P.H., Veterans Affairs Connecticut Healthcare System, Building 35A, Room 201, 950 Campbell Avenue, West Haven, CT 06516-2770. E-mail: lori.bastian@va.gov.

Ann Am Thorac Soc Vol 17, No 10, pp 1273–1278, Oct 2020

Copyright © 2020 by the American Thoracic Society

DOI: 10.1513/AnnalsATS.201910-750OC

Internet address: www.atsjournals.org

Obstructive sleep apnea (OSA) is a prevalent condition of complete or partial upper airway obstruction during sleep. Overall, 10–17% of men and 3–9% of women in the United States have moderate to severe OSA (1). The prevalence of OSA in male veterans

has doubled over the past 10 years (2) and is reported to be twice as prevalent compared with that in the general population (3, 4). Risk factors associated with OSA include male sex, older age (40–70 years), postmenopausal status, obesity, craniofacial

abnormalities, smoking, posttraumatic stress disorder (PTSD), and central nervous system depressant use (5).

Veterans frequently report significant musculoskeletal pain (6–8). The specific link between OSA and pain remains unclear, but

one hypothesis posits that patients with OSA become hyperalgesic because of fragmented sleep, thereby enhancing sensitivity to pain, promoting inflammation, and advancing spontaneous pain (9–11). It is also believed that this association may be bidirectional, with an increase in pain and opioid use shown to be associated with sleep-disordered breathing (12, 13). In addition, OSA is associated with the development and progression of headaches (14). Most studies examining the association of OSA and pain intensity have included older (age 50 years and above) patients, so there is a need to understand the relationship between OSA and pain among younger adults and to examine for potential sex differences (11).

This cohort of veterans presents a unique opportunity to explore the patterns and correlates of OSA and pain intensity in predominantly young group of veterans who used the Veterans Health Administration (VHA) national system of care. We aimed to 1) characterize the patterns and prevalence of OSA in young adults and 2) examine the association of OSA and moderate/severe pain intensity, adjusting for factors such as smoking status, mental health diagnoses (PTSD, depression, and substance use), headache diagnoses, pain diagnoses, hypertension, diabetes, benzodiazepine/opioid prescription, and obesity that may be differentially associated with these outcomes in men and women. This article was presented in part at the American Thoracic Society 2018 International Conference on May 19, 2018, in San Diego, California, and at the Society of General Internal Medicine 2019 Annual Meeting on May 10, 2019 in Washington, District of Columbia.

Methods

Study Design/Population

The sampling frame for the overall study is the Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn roster, provided to the VHA as reported previously (15). The data include a list of veterans enrolled in Veterans Affairs (VA) health care between October 1, 2001, and September 30th, 2014 ($n = 1,063,973$). It includes information on veterans' sex, race, education, date of birth, date of last deployment, branch of service, and rank. Our analyses included only patients with

one or more VHA primary care visits ($n = 858,226$). The study was approved by the institutional review boards at VA Connecticut Healthcare System and Yale University School of Medicine.

Data Sources

Data on eligible patients were linked to VHA administrative and clinical data contained within the Corporate Data Warehouse. These databases provide a record of inpatient and outpatient healthcare encounters, pharmacy data, and coded diagnostic conditions (based on the *International Classification of Diseases, Ninth Revision* [ICD-9]).

OSA Diagnosis

ICD-9 codes were used to identify OSA. OSA was identified using one inpatient or two outpatient ICD-9 codes from electronic medical records (16). We included the OSA code (327.23), unspecified sleep apnea code (780.57), and insomnia with sleep apnea code (780.51). We also included organic sleep apnea, unspecified (327.20), and other organic sleep apnea (327.29). These ICD-9 codes for OSA have been validated in prior studies (17, 18).

Outcome: Pain Intensity

Patients are screened for the presence and intensity of pain using a 0–10 numeric rating scale at every primary care clinic visit. Patients are asked to “rate your current pain on a 0 (no pain) to 10 (worst pain imaginable)” scale, and the response is recorded in the veteran's electronic medical record (EMR). We averaged pain intensity measures over a 12-month time period before the most recent outpatient or inpatient visit that measured pain intensity. Average pain intensity was categorized as none (0), mild (1–3), and moderate/severe (4–10). (19)

Covariates

Demographic variables, including age, age categories (less than 30 years old, 30–39 years old, and 40 or more years old), sex, race/ethnicity (e.g., Black, Hispanic, other/unknown, and white), and education (high school diploma or the equivalent and greater than high school), were examined.

Smoking status was categorized as current, former, or never-smokers based on a comprehensive algorithm using keywords (e.g., current smoker, never-smoker, and tobacco counseling) found in text entries

and results from clinical reminders in the Corporate Data Warehouse (20). We included the most recent smoking status relative to the primary care visit of interest.

Headache Diagnoses

We included diagnostic code groupings for headache conditions (e.g., migraine and tension headache) using the ICD-9 codes 346, 307.81, and 784 (7).

Pain Diagnoses

We included diagnostic code groupings for pain diagnoses, including back pain, osteoarthritis, fibromyalgia, and temporomandibular disorders, using the ICD-9 codes 721, 722, 724, 839, 715, 729.1, and 524 (7).

Chronic Medical Conditions

We included the ICD-9 diagnostic code groupings for the following two common medical conditions: hypertension (401–405 and 437.2) and diabetes (250).

Mental Health Diagnoses

We used the Agency for Healthcare Research and Quality's Clinical Classifications Software ICD-9 codes to identify mental health conditions (21). We examined the following mental health conditions based on their relatively high prevalence in veteran populations and their frequent comorbidity with painful conditions: major depressive disorder, PTSD, and substance use (alcohol and illicit drug use).

Benzodiazepines/Opioid Prescriptions

We selected “any prescription” defined as at least one filled prescription for opioids and/or benzodiazepines in the VHA prescription data within ± 90 days of OSA diagnosis.

Body Mass Index

The most recent body mass index (BMI) (in kg/m^2) relative to the date of OSA diagnosis was extracted using the height and weight recorded in the EMR. Using standard classifications, patients were categorized as obese (BMI of 30 or more) or nonobese (BMI of less than 30) (22).

Analysis

We used bivariate associations to compare patient characteristics, including pain intensity, with OSA diagnosis (yes/no). Multivariate logistic regression analyses

were used to examine the association of OSA with pain intensity (moderate/severe pain intensity vs. other), controlling for potential confounders such as age, race, sex, education, mental health diagnoses, smoking status, headache diagnoses, pain diagnoses, hypertension, diabetes, and obesity. These covariates were selected for their known association with OSA and/or pain intensity. We used multiple imputation (using SAS multiple imputation procedure_ to account for missing data from race/ethnicity ($n = 12,459$; 1.5%), BMI ($n = 71,174$; 8.3%), and smoking variables ($n = 116,023$; 13.5%) (23). The imputation model included age, sex, smoking status, race/ethnicity, diabetes, hypertension, major depression, PTSD, substance use disorder, BMI, OSA, headache, pain diagnoses, and education. Ten datasets were imputed, and the MIANALYZE procedure in SAS was used to combine odds ratio estimates. We conducted a sensitivity analysis comparing the results of a complete case analysis with the imputed result and found no substantial differences. We chose to report results of the multivariable model using imputed data (24). We also conducted a subgroup analysis to examine potential sex differences and conducted sensitivity analyses to examine the association of OSA and pain intensity among important subgroups including obesity, benzodiazepine/opioid prescription use, and categories of chronic disease. All statistical analyses were performed using SAS version 9.4 (SAS, Inc).

Results

We identified 858,226 Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn veterans who met our inclusion criteria. The mean age of our sample was 30 years ($SD = 9.14$), and 64.4% were white, 16.5% were Black, 11.6% were Hispanic, and 7.6% were other/unknown race/ethnicity. The majority of our sample (90%) was male and 20% had greater than a high school education.

We identified 91,244 (10.6%) young adults with an OSA diagnosis. There were several differences between patients with and without OSA (Table 1). Compared with those without OSA, those with OSA were older (36 years old vs. 26 years old), were more likely to be Black, male, married, obese, and a never-smoker, and were more

likely to have greater than a high school education. Patients with OSA were also more likely to endorse moderate to severe pain intensity (35.2% vs. 26.8%), have a pain diagnosis (36.2% vs. 16.3%), and have a headache diagnosis (28.0% vs. 14.0%). Patients with OSA were also more likely to have a diagnosis of diabetes (12.1% vs. 2.4%) and hypertension (40% vs. 12%). Major depressive disorder (19.6% vs. 9.9%), PTSD (49.9% vs. 30.3%), and substance use disorder (26.2% vs. 16.9%) were more common among patients with OSA. Patients with OSA were also more likely to have been prescribed benzodiazepines or opioids within 90 days of OSA diagnosis.

Compared with patients without OSA, the unadjusted odds of reporting moderate/severe pain were 48% higher (95% confidence Interval CI, 1.46–1.51) for those with OSA (Table 2). After adjusting for all covariates in the model (Table 2), the association between OSA and moderate/severe pain remained significant, although the effect was significantly attenuated (adjusted odds ratio, 1.09; 95% CI, 1.08–1.11). Of note, the association between OSA and moderate/severe pain was stronger (adjusted odds ratio, 1.17; 95% CI, 1.15–1.19) when pain diagnoses were not included in the model (data not otherwise shown).

Table 1. Characteristics of veterans by OSA status ($N = 858,226$)

Characteristic	Patients with OSA ($n = 91,244$)	Patients without OSA ($n = 766,982$)	P Value
Age, yr (IQR)	36 (27–42)	26 (22–35)	<0.0001
Age categories, yr			<0.0001
Less than 30	33.3	63.7	—
30–39	33.3	20.1	—
40 and greater	33.4	16.2	—
Sex, M, %	94.9	86.7	<0.0001
Race, %			<0.0001
White	54.8	65.5	—
Black	23.6	15.6	—
Hispanic	13.5	11.4	—
Other	8.1	7.5	—
Married	68.9	46.8	<0.0001
Education, %			
≥High school	26.5	20.4	<0.0001
Body mass index ≥30 kg/m ² , %	68.6	34.5	<0.0001
Smoking			<0.0001
Current	31.9	38.4	—
Former	19.4	16.8	—
Never	48.7	44.8	—
Average pain intensity, median (IQR)	2.75 (0.75–5)	1.67 (0–4)	<0.0001
Average pain intensity after excluding no pain, median (IQR)	3.5 (2–5)	3.1 (2–5)	<0.0001
Pain intensity, %			<0.0001
None	20.3	35.5	—
Mild (1–3)	44.5	37.7	—
Moderate to severe (4–10)	35.2	26.8	—
Mental health diagnoses, %			
Depression	19.6	9.9	<0.0001
Posttraumatic stress disorder	49.9	30.3	<0.0001
Substance use	16.8	14.1	<0.0001
Anxiety disorder	26.2	16.9	<0.0001
Headache diagnosis, %	28.0	14.0	<0.0001
Pain diagnosis, %	36.2	16.3	<0.0001
Hypertension, %	40.0	12.0	<0.0001
Diabetes, %	12.1	2.4	<0.0001
Opioid/Benzodiazepine prescriptions ± 90 d of OSA diagnosis, %			
Opioids	13.3	8.8	<0.0001
Benzodiazepines	6.6	3.7	<0.0001

Definition of abbreviations: IQR = interquartile range; OSA = obstructive sleep apnea.

Table 2. Association between OSA diagnosis and moderate/severe pain intensity (N = 858,226)

	No/Mild Pain	Moderate/Severe Pain	P Value
Subjects, <i>n</i>	619,639	238,587	—
Subjects with OSA, <i>n</i>	59,126	32,118	—
Prevalence of OSA, % (95% CI)	9.5 (9.4–9.6)	13.5% (13.4–13.6)	<0.0001
Unadjusted odds ratio of OSA (95% CI)	1 (Ref)	1.48 (1.46–1.51)	<0.0001
Adjusted* odds ratio of OSA (95% CI)	1 (Ref)	1.09 (1.08–1.11)	<0.0001

Definition of abbreviations: CI = confidence interval; OSA = obstructive sleep apnea; Ref = reference value.

*Adjusted for age categories (<30, 30–39, and ≥40 years old), sex, race (nonwhite vs. other), education (post-high school vs. other), posttraumatic stress disorder, major depression, smoking status (never, former, and current), body mass index (≥30 kg/m² vs. other), headache diagnoses, pain diagnoses, hypertension, and diabetes.

In a subgroup analysis by sex (Table 3), moderate/severe pain intensity was observed among both men and women with a diagnosis of OSA. In additional sensitivity analyses stratified by obesity, pain diagnoses, and benzodiazepine/opioid prescription use, the associations between OSA and moderate/severe pain were essentially unchanged. Finally, we did not find a significant interaction term between sex, OSA, and pain intensity (data not otherwise shown).

Discussion

We found younger adults with an OSA diagnosis were more likely to report moderate to severe pain intensity compared with patients without an OSA diagnosis even after adjusting for several key confounders known to be associated with OSA and pain intensity. Given the relatively

young age of this cohort, this relationship between OSA and pain is quite interesting and warrants further exploration. Our study is the first to evaluate this relationship between OSA and pain in young adults on such a large scale, and our findings warrant further exploration of the effects of OSA treatment with continuous positive airway pressure (CPAP) and/or mandibular advancement devices and subsequent changes with respect to pain severity.

Participants with mental health diagnoses, such as depression and PTSD, reported higher rates of OSA diagnosis. Previous studies have reported that the incidence of OSA is higher in patients with depression, PTSD, bipolar disorder, and anxiety than in the general population (25). In a prospective study of 115 patients with depression undergoing a sleep study, OSA was diagnosed in more than 50% of patients (26).

Our results also support the complex relationship between substance use (alcohol

and drug use) and OSA. Previous studies have found that patients with alcohol use and tobacco use have more severe OSA (27). The high prevalence of pain symptoms among patients with OSA could also be related to comorbid substance use and depression, but here, we show that even after multivariable adjustment, the association of OSA with pain remains independent.

Obesity is a known risk factor for both OSA and chronic pain. In a retrospective evaluation of patients attending a pain management clinic, the prevalence of OSA was 13.8% (28). The prevalence of OSA is associated with BMI, with 32.4% in morbidly obese patients compared with 5.7% in those with normal weight. It has been suggested that obesity increases the prevalence of pain by increasing inflammatory markers and increasing the risk of osteoarthritis, whereas pain frequently reduces physical activity that can result in increased BMI (29).

Although men were more likely to have a diagnosis of OSA, we did not find sex differences in the association of OSA and pain in our sex-based stratified analyses. A study of 101 women in the military referred for a sleep study found that OSA was diagnosed in 50%, which is higher than the previously reported 16–21% (30). In this study, it was noted that women who were referred for sleep studies were particularly prone to have mental health and pain disorders. Furthermore, it has been noted that female patients with OSA have different types of complaints than male patients with OSA. Specifically, women will typically complain of insomnia, headache, irritability, and fatigue rather than the classic symptoms of snoring and/or apnea that are seen in men

Table 3. Association between OSA diagnosis and moderate/severe pain intensity (N = 858,226) stratified by sex

	Men (N = 751,435)			Women (N = 106,791)		
	No/Mild Pain	Moderate/Severe Pain	P Value	No/Mild Pain	Moderate/Severe Pain	P Value
Number of subjects	539,490	211,945	—	77,891	24,247	—
Number with OSA	56,125	30,466	—	2,970	1,683	—
Prevalence of OSA, % (95% CI)	10.4 (10.3–10.5)	14.4 (14.3–14.5)	<0.0001	3.6 (3.5–3.7)	6.5 (6.2–6.8)	<0.0001
Unadjusted odds ratio of OSA (95% CI)	1 (Ref)	1.45 (1.42–1.47)	<0.0001	1 (Ref)	1.82 (1.71–1.94)	<0.0001
Adjusted* odds ratio of OSA (95% CI)	1 (Ref)	1.10 (1.08–1.12)	<0.0001	1 (Ref)	1.09 (1.02–1.17)	0.0009

Definition of abbreviations: CI = confidence interval; OSA = obstructive sleep apnea; Ref = reference value.

*Adjusted for age categories (<30, 30–39, and ≥40 years old), Race (nonwhite vs. other), education (post-high school vs. other), posttraumatic stress disorder, major depression, smoking status (never, former, and current), body mass index (≥30 kg/m² vs. other), headache diagnoses, pain diagnoses, hypertension, and diabetes.

(31). Future research should examine for potential sex differences in the OSA and pain relationship by broader age strata.

Chronic headache is a particularly common condition in patients with an OSA diagnosis. A specific type of headache, the morning “sleep apnea headache” when awakening from sleep, is considered to be caused by OSA and can raise a clinician’s suspicion for OSA. In previous studies, morning headache was significantly more frequent among patients with OSA than those without OSA (32). Even though the association of OSA with other primary headaches, such as migraine, is unclear and has been debated (31), treating OSA leads to clinically important improvement in over 30% of patients with undifferentiated chronic headache (33). In our study, the prevalence of headache diagnoses in patients with OSA was twice that of patients without OSA.

Pain diagnoses, including back pain, osteoarthritis, fibromyalgia, and temporomandibular disorders, were more common in patients with OSA. Patients with these diagnoses may not always report moderate/severe pain intensity. Because pain diagnoses are commonly managed and pain intensity is routinely ascertained in

primary care, this might serve as an opportunity to assess patients for OSA risk factors and related symptoms.

There are some limitations to consider when evaluating this study. First, this was a cross-sectional examination of a large database, which limits our ability to draw conclusions about causation. We relied on self-reported measures of smoking, although we note that self-reported smoking status in the VHA EMR has been validated in previous studies (20). We used the average of a one-item measure of pain intensity over a 12-month period, which does not capture the full range of complexity of pain as a construct (34). We included ICD-9 diagnoses to describe the cohort and may have missed diagnoses if providers did not code them in the VHA EMR. Future research would benefit from more detailed assessments of pain, including measures of the quality, duration, and location of pain, as well as pain treatments and pain-related functional interference.

Based on these results, we suggest more thorough and more frequent pain intensity screening in patients with OSA, particularly in those patients who are younger than 60 years old without significant comorbid illness. Furthermore, we also recommend

increased OSA screening for patients with moderate/severe pain intensity and pain diagnoses. The STOP-Bang (Snoring, Tiredness, Observed apnea, blood Pressure, Body mass index, Age, Neck circumference, and Gender) questionnaire has been validated in multiple settings and can serve as a simple but effective tool for evaluation in the primary care setting (35). In future studies, we plan to examine the role of CPAP in modulating the relationship between OSA and pain, specifically examining the effect of CPAP adherence on pain intensity in young adults.

This national study highlights the importance of understanding the association between OSA and pain among younger adults. Because of the high burden of chronic pain conditions in younger adults, this study highlights the need to understand the impact of OSA diagnosis and treatment on pain intensity. This understanding would then help inform the development of interventions to promote screening for OSA among young adults with chronic pain and pain management among those with diagnosed OSA. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

References

- Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol* 2013;177:1006–1014.
- Jackson M, Becerra BJ, Marmolejo C, Avina RM, Henley N, Becerra MB. Prevalence and correlates of sleep apnea among US male veterans, 2005–2014. *Prev Chronic Dis* 2017;14:E47.
- Mustafa M, Erokwu N, Ebose I, Strohl K. Sleep problems and the risk for sleep disorders in an outpatient veteran population. *Sleep Breath* 2005;9:57–63.
- Ocasio-Tascón ME, Alicea-Colón E, Torres-Palacios A, Rodríguez-Cintrón W. The veteran population: one at high risk for sleep-disordered breathing. *Sleep Breath* 2006;10:70–75.
- Colvonen PJ, Masino T, Drummond SPA, Myers US, Angkaw AC, Norman SB. Obstructive sleep apnea and posttraumatic stress disorder among OEF/OIF/OND veterans. *J Clin Sleep Med* 2015;11:513–518.
- Haskell SG, Brandt CA, Krebs EE, Skanderson M, Kerns RD, Goulet JL. Pain among Veterans of Operations Enduring Freedom and Iraqi Freedom: do women and men differ? *Pain Med* 2009;10:1167–1173.
- Higgins DM, Kerns RD, Brandt CA, Haskell SG, Bathulapalli H, Gilliam W, et al. Persistent pain and comorbidity among Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn veterans. *Pain Med* 2014;15:782–790.
- Hyams KC, Wignall FS, Roswell R. War syndromes and their evaluation: from the U.S. Civil War to the Persian Gulf War. *Ann Intern Med* 1996;125:398–405.
- Khalid I, Roehrs TA, Hudgel DW, Roth T. Continuous positive airway pressure in severe obstructive sleep apnea reduces pain sensitivity. *Sleep (Basel)* 2011;34:1687–1691.
- Doufas AG, Tian L, Davies MF, Warby SC. Nocturnal intermittent hypoxia is independently associated with pain in subjects suffering from sleep-disordered breathing. *Anesthesiology* 2013;119:1149–1162.
- Charokopos A, Card ME, Gunderson C, Steffens C, Bastian LA. The association of obstructive sleep apnea and pain outcomes in adults: a systematic review. *Pain Med* 2018;19(suppl_1):S69–S75.
- Lettieri CJ, Eliasson AH, Andrada T, Khramtsov A, Raphaelson M, Kristo DA. Obstructive sleep apnea syndrome: are we missing an at-risk population? *J Clin Sleep Med* 2005;1:381–385.
- Hassamal S, Miotto K, Wang T, Saxon AJ. A narrative review: the effects of opioids on sleep disordered breathing in chronic pain patients and methadone maintained patients. *Am J Addict* 2016;25:452–465.
- Olmos SR. Comorbidities of chronic facial pain and obstructive sleep apnea. *Curr Opin Pulm Med* 2016;22:570–575.
- Volkman JE, DeRycke EC, Driscoll MA, Becker WC, Brandt CA, Mattocks KM, et al. Smoking status and pain intensity among OEF/OIF/OND Veterans. *Pain Med* 2015;16:1690–1696.
- Fultz SL, Skanderson M, Mole LA, Gandhi N, Bryant K, Crystal S, et al. Development and verification of a “virtual” cohort using the National VA Health Information System. *Med Care* 2006;44(Suppl 2):S25–S30.
- Alexander M, Ray MA, Hébert JR, Youngstedt SD, Zhang H, Steck SE, et al. The national veteran sleep disorder study: descriptive epidemiology and secular trends, 2000–2010. *Sleep (Basel)* 2016;39:1399–1410.
- Kunisaki KM, Akgün KM, Fiellin DA, Gibert CL, Kim JW, Rimland D, et al. Prevalence and correlates of obstructive sleep apnoea among patients with and without HIV infection. *HIV Med* 2015;16:105–113.
- Goulet JL, Brandt C, Crystal S, Fiellin DA, Gibert C, Gordon AJ, et al. Agreement between electronic medical record-based and self-administered pain numeric rating scale: clinical and research implications. *Med Care* 2013;51:245–250.
- McGinnis KA, Brandt CA, Skanderson M, Justice AC, Shahrir S, Butt AA, et al. Validating smoking data from the Veteran’s Affairs Health

Factors dataset, an electronic data source. *Nicotine Tob Res* 2011;13:1233–1239.

- 21 Elixhauser A, Steiner C, Palmer L. Clinical Classifications Software (CCS), for ICD-9-CM. 1995 [accessed 2020 Jun 2]. Available from: <http://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp>.
- 22 Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. National Institute of Health. *Obes Res* 1998;6(Suppl 2):51S–209S.
- 23 Little RJA, Rubin DB. Statistical analysis with missing data, 2nd ed. Hoboken, NJ: John Wiley & Sons; 2014.
- 24 Hausmann LRM, Brandt CA, Carroll CM, Fenton BT, Ibrahim SA, Becker WC, et al. Racial and ethnic differences in total knee arthroplasty in the Veterans Affairs Health Care System, 2001–2013. *Arthritis Care Res (Hoboken)* 2017;69:1171–1178.
- 25 Szaulińska K, Plywaczewski R, Sikorska O, Holka-Pokorska J, Wierzbicka A, Wichniak A, et al. Obstructive sleep apnea in severe mental disorders [in English, Polish]. *Psychiatr Pol* 2015;49:883–895.
- 26 Cai L, Xu L, Wei L, Sun Y, Chen W. Evaluation of the risk factors of depressive disorders comorbid with obstructive sleep apnea. *Neuropsychiatr Dis Treat* 2017;13:155–159.
- 27 Stelmach-Mardas M, Mardas M, Iqbal K, Kostrzewska M, Piorunek T. Dietary and cardio-metabolic risk factors in patients with obstructive sleep apnea: cross-sectional study. *PeerJ* 2017;5:e3259.
- 28 Pampati S, Manchikanti L. What is the prevalence of symptomatic obstructive sleep apnea syndrome in chronic spinal pain patients? An assessment of the correlation of OSAS with chronic opioid therapy, obesity, and smoking. *Pain Physician* 2016;19:E569–E579.
- 29 McCarthy LH, Bigal ME, Katz M, Derby C, Lipton RB. Chronic pain and obesity in elderly people: results from the Einstein aging study. *J Am Geriatr Soc* 2009;57:115–119.
- 30 Capener DC, Brock MS, Hansen SL, Matsangas P, Mysliwiec V. An initial report of sleep disorders in women in the U.S. Military. *Mil Med* 2018;183:e266–e271.
- 31 Stark CD, Stark RJ. Sleep and chronic daily headache. *Curr Pain Headache Rep* 2015;19:468.
- 32 Kristiansen HA, Kværner KJ, Akre H, Øverland B, Sandvik L, Russell MB. Sleep apnoea headache in the general population. *Cephalalgia* 2012;32:451–458.
- 33 Poceta JS, Dalessio DJ. Identification and treatment of sleep apnea in patients with chronic headache. *Headache* 1995;35:586–589.
- 34 Goulet JL, Buta E, Bathulapalli H, Gueorguieva R, Brandt CA. Statistical models for the analysis of zero-inflated pain intensity numeric rating scale data. *J Pain* 2017;18:340–348.
- 35 Nagappa M, Liao P, Wong J, Auckley D, Ramachandran SR, Memtsoudis S, et al. Validation of the STOP-bang questionnaire as a screening tool for obstructive sleep apnea among different populations: a systematic review and meta-analysis. *PLoS One* 2015;10:e0143697.