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SCIENTIFIC INVESTIGATIONS

Associations of Undiagnosed Obstructive Sleep Apnea and Excessive Daytime Sleepiness With Depression: An Australian Population Study

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Study Objectives: To determine whether undiagnosed obstructive sleep apnea (OSA) and/or excessive daytime sleepiness are associated with symptomatic depression in Australian men.

Methods: Participants were randomly selected, urban community dwelling men aged 40 to 88 years without a prior diagnosis of OSA. Clinically significant depressive symptoms were assessed using the Beck Depression Inventory-1A or Centre for Epidemiological Studies Depression Scale (2007–2010). A random sample of men (n = 788) undertook full at-home unattended polysomnography (Embletta X100, Broomfield, Colorado, United States) and completed the Epworth Sleepiness Scale questionnaire (2010–2012).

Results: Undiagnosed severe obstructive sleep apnea (apnea-hypopnea index ≥ 30 events/h) was associated with depressive symptoms (adjusted odds ratio = 1.98; 95% confidence interval [CI] 1.05–3.73; *P* = .036). However, a significant interaction was observed between obstructive sleep apnea and excessive daytime sleepiness (*P* = .03) such that individuals with OSA and excessive daytime sleepiness (Epworth Sleepiness Scale score of 10 or higher) exhibited the strongest associations with depression (mild–moderate apnea: adjusted odd ratio = 3.86; 95% CI 1.87–7.95; severe apnea: adjusted odd ratio = 4.82; 95% CI 1.42–16.35) when compared to individuals without apnea.

Conclusions: Depressive symptoms in men were associated with undiagnosed OSA in the community. It is important that clinicians and primary care practitioners consider screening for depression in men with severe OSA and for OSA in men with depression. Screening for depression should also be considered in men with excessive daytime sleepiness regardless of OSA severity.

Keywords: depression, epidemiology, obstructive sleep apnea, polysomnography, population based community cohort, somnolence

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INTRODUCTION

Depression is a serious health concern, with 6.9% of people in the United States experiencing a major depressive episode each year.[1] In both the United States and Australia, around 5% of adult males are affected.[1,2] Men are less likely to seek, and more likely to drop out of, treatment for their depression and are four times more likely to commit suicide than females.[3] A wide variety of demographic and lifestyle factors have been associated with depression.[2–5] Obesity, anxiety, insomnia, cardiovascular disease, diabetes, and lower urinary tract symptoms are conditions associated with an increased risk of depression and these have also been linked to sleep disorders[2,5,6]; the most common sleep disorder in men is obstructive sleep apnea (OSA).

OSA has been estimated to affect 49% of middle-aged men.[7] OSA is sometimes accompanied by daytime sleepiness and fatigue. There is a high prevalence of depression in patients with OSA (eg, 15% to 24% in population studies[8,9] and 39% in clinic studies[10]). Few studies have been undertaken in community-based populations. One key exception is the Wisconsin Sleep Cohort Study[9] that reported a longitudinal

BRIEF SUMMARY

Current Knowledge/Study Rationale: A high prevalence of depressive symptoms occurs in patients with obstructive sleep apnea (OSA); however, studies investigating associations between depression and OSA have yielded mixed results. Many referred clinic studies indicate no association between the disorders and a few retrospective studies report that there is. To date, there have been very few studies undertaken in community-based populations.

Study Impact: Sleep clinicians and general health practitioners should be particularly alert to the risk of comorbid OSA and depression in the community. Although our findings indicate that the risk for depression is highest in men with both OSA and excessive daytime sleepiness who make up 2.0% of the men in our study population, the much larger group of men (11%) who have severe apnea without excessive daytime sleepiness still have an almost twofold increased risk of depression and constitute a significant problem in population health because they may be less likely to seek medical advice for their condition.

dose-dependent association between sleep-related breathing disorders and at least mild depression in a working population of men and women. Interestingly, daytime sleepiness did not influence the association of OSA and depression.[9]

Up to 82% of men affected by OSA remain undiagnosed.[11] Untreated OSA presents a considerable socioeconomic burden, including deleterious effects on physical health outcomes, as well as increased rates of health care utilization, medication use, motor vehicle accidents, and income loss.[12] Daytime sleepiness is regarded as a cardinal symptom of significant OSA and often drives investigation and treatment. Sleepiness is also associated with depression. However, in randomized controlled trials continuous positive airway pressure treatment of OSA does not always improve depression[13] and residual sleepiness after continuous positive airway pressure treatment has been found to be associated with persistent depression.[14,15] If sleepiness does not affect the relationship between OSA and depression, as reported in the Wisconsin Sleep Cohort Study,[9] this would have implications for identifying and treating people with OSA and depression. Thus there still remains a significant gap in our knowledge as to the extent of the burden of depression in men with undiagnosed, and therefore untreated, OSA in the community. This study sought to determine the extent to which undiagnosed OSA might account for cases of depression in the community. We further sought to determine the role of excessive daytime sleepiness (EDS) in modifying any cross-sectional relationship between undiagnosed OSA and depression.

METHODS

Study Participants

The Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) study includes randomly selected community-dwelling men of largely Australian or European descent (96%) aged at least 35 years at baseline (2002–2006) and has been described previously.[16] The MAILES study consists of the harmonization of two concurrent, biomedical, random population cohorts that were historically identified as the Florey Adelaide Male Ageing Study (FAMAS) and the North West Adelaide Health Study (NWAHS). Both the FAMAS and NWAHS used the same methodology and sample frame for initial recruitment. The main difference between the two studies is that NWAHS recruited for both sexes. MAILES participants were very similar to respondents in the nationally representative Men in Australia Telephone Survey across a range of sociodemographic, physical, and health characteristics.[16] All components of the MAILES study were approved by the Royal Adelaide Hospital Research Ethics Committee and North West Adelaide Health Service Ethics of Human Research Committee, and all subjects gave written informed consent.

Participants completed clinical assessments and a computer-assisted telephone interview (n = 1,629).[16] Subjects reporting "No" when asked "Have you ever been diagnosed with OSA with a sleep study?" during the computer-assisted telephone interview were invited to undergo a sleep study (September 2010–February 2012). Overall, 75.2% (1,087 of 1,445 without a previous OSA diagnosis) initially agreed to participate. Of these, a random sample (n = 857) underwent polysomnography. The comparison of MAILES subjects who did and did not undertake polysomnography has previously been reported.[17] Minor healthy volunteer bias was seen with sleep study participants, who on average were younger (mean ± standard deviation: 60 ± 11 years versus 62 ± 12 years), less obese, and less likely to report poor general health, but did not differ otherwise from nonparticipants in sleep symptoms (sleepiness, frequency of waking) or OSA risk (STOP [snoring, tiredness, observed apnea, high blood pressure] questionnaire), or socioeconomic status.

Clinical Assessments

Self-completed questionnaires were used to collect detailed demographic and risk factor information.[16,17] Biomedical assessment was conducted in hospital-based clinics, using standardized and reproducible study protocols previously described.[16,17] Briefly, body mass index (BMI; kg/m^2) was categorized according to international criteria: underweight/normal ≤ 24.9; overweight 25–29.9, obese ≥ 30. Waist circumference (WC) measurements were the mean of 3 measurements. Central obesity was identified using the following WC categories: obese WC ≥ 102 cm; overweight: WC 95–101 cm, healthy: WC < 95 cm. Diabetes was determined by self-report of doctor diagnosis, fasting plasma glucose ≥ 7.0 mmol/L or hemoglobin A1c ≥ 6.5%. Cardiovascular disease included self-reported, doctor-diagnosed myocardial infarction, stroke, transient ischemic attack, or angina. Joint pain (from osteoarthritis or rheumatoid arthritis, or both) was self-reported. Erectile dysfunction were identified using the International Index of Erectile Dysfunction Global Impotence Rating, with moderate and severe combined. Depression was assessed using the Centre for Epidemiological Studies Depression Scale (CES-D) if the participant was historically part of the NWAHS cohort (n = 352) or the Beck Depression Inventory-1A (BDI-1A) if the participant was historically part of the FAMAS cohort (n = 399). The cutoff points (CES-D, 16; BDI-1A, 10) used for both scales have been shown to identify "clinically significant depressive symptoms," termed here as depression.[18,19]

Sleep Study

Trained staff visited participants in their homes to set up and attach eight-channel in-home unattended polysomnography (Embletta X100, Broomfield, Colorado, United States) to measure electroencephalography, electro-oculography, electromyelography, nasal pressure, thoracic and abdominal effort, oximetry, and body position. Failed studies (n = 40) were repeated, generating a final sample of 837. All polysomnography studies were scored by a single experienced sleep technician according to 2007 American Academy of Sleep Medicine (alternative) criteria[20] as previously described.[17] OSA was defined as an apnea-hypopnea index (AHI) ≥ 10 events/h of sleep, with further categorization; mild: AHI of 10 to 19 events/h, moderate: 20 to 29 events/h, and severe: ≥ 30 events/h.[21] These cutoffs were chosen as previous work suggests that the AHI cutoff of 5 events/h used to define sleep-disordered breathing in the Wisconsin Sleep Cohort Study[9] is approximately equivalent to an AHI of 10 events/h using the alternate American Academy

Table 1—Summary characteristics of all, nondepressed, and depressed participants.

	All Participants	Men with No Depressive Symptoms	Men with Depressive Symptoms	ANOVA *F*	*P*
n (%)	788 (100)	677 (86)	111 (14)		
Age (y)	58.10 ± 10.78	58.14 ± 10.92	57.82 ± 9.96	0.086	.769
WC (cm)	99.54 ± 11.57	99.35 ± 11.53	100.65 ± 11.83	1.207	.272
BMI (kg/m^2)	28.47 ± 4.20	28.41 ± 4.13	28.79 ± 4.60	0.775	.379

ANOVA = analysis of variance, BMI = body mass index, WC = waist circumference.

of Sleep Medicine definition.[21] We used the number of oxygen desaturation measurements of 3% or more per hour (3% oxygen desaturation index [ODI 3%]) as the indicator of nocturnal intermittent hypoxia, with ODI 3% < 5, between 5 and 24, and ≥ 25 events/h, corresponding to mild, moderate, and severe nocturnal intermittent oxygen desaturation, respectively, and the percentage of sleep time with oxygen saturation less than 90% as the primary indicator for nocturnal hypoxemia. On the night of the sleep study participants completed the Epworth Sleepiness Scale questionnaire and medication use and reasons for taking a medication were recorded (which allowed us to adjust for any new medicated cases of depression within the study time frame). EDS was defined as an Epworth Sleepiness Score higher than 10.[22] A physician investigator coordinated any necessary clinical follow-ups and the results were made available to participants and, with the participant consent, to their primary care practitioner.

Statistical Analyses

Differences in demographics among men with or without depressive symptoms were assessed using chi-square (χ^2) and *t* tests, where appropriate. Binomial logistic regressions were employed to assess the relationships between OSA, EDS, OSA stratified by EDS, and other risk factors for depression. The pairwise interaction between OSA and EDS was assessed using log-likelihood ratio tests comparing nested models with and without the interaction. These analyses included OSA and sleepiness as continuous variates using log-transformed AHI for OSA and the Epworth Sleepiness Scale for sleepiness. In addition, a composite OSA-EDS variable (6 levels: OSA = none versus mild–moderate versus severe crossed with EDS = yes versus no) was included to estimate the prevalence of depression in individuals with severe OSA with or without EDS. To control for economic status we used a measure of financial stress (assessing disposable income) rather than annual household income, which is not independent of demands. Similarly, WC was used in favor of BMI measurement in the final model due to its closer relationship with total body fat and cardio-metabolic risk in men. A sensitivity analyses was performed including BMI instead of WC, resulting in qualitatively similar results. Because 2 different questionnaires were used to assess depression status depending on the history of the 2 cohorts that were merged to form the MAILES study, we used a categorical (yes/no) depression variable as our dependent variable, and questionnaire type was included as a confounder. Further, we conducted a sensitivity analysis for each questionnaire both independently and together using the square-root transformed depression scores as a continuous outcome variable in linear regressions. We also assessed whether the time differences between depression assessment and the sleep study influenced the associations by including a time difference variable in the linear and logistic regressions. Data were analyzed using SPSS version 20 (SPSS Inc., Chicago, Illinois, United States) and R version 3.2.0 (2015, R Development Core Team, http://www.r-project.org/, United States).

RESULTS

Of the 857 men participating in the sleep study, 837 had successful studies. Of these, 788 completed one of the depression questionnaires. There were 29 men taking medications for depression or mood problems at the time of the sleep study and these men were included as depressed. The biodemographic and sleep characteristics of the male participants of this cohort, and in relation to depression prevalence, are presented in **Table 1** and **Table 2**. The percentage of men with EDS was independent of OSA severity (no OSA: 12%; mild–moderate OSA: 14%; severe OSA: 14%). Depression was associated with undiagnosed severe OSA, EDS (Epworth Sleepiness Scale score higher than 10), erectile dysfunction, not being in a relationship (ie, married or living with a partner), and financial strain, in both unadjusted and multivariable models (**Table 2** and **Table 3**, respectively). Polysomnography parameters including oxygen desaturation index, total sleep time with oxygen saturation less than 90%, and arousal index were not significantly associated with depression (**Table 2**). There was a significant interaction between OSA and EDS ($P = .03$) in which individuals with mild–moderate or severe OSA and EDS exhibited increased probability of depression compared to individuals with either condition alone (**Figure 1**). When adjusting for financial strain, marital status, age, WC, current smoking, and erectile dysfunction, men with either mild–moderate or severe OSA and EDS had a greater likelihood of also having had depression compared with men without either OSA or EDS (**Table 4**). The association of severe OSA without sleepiness with depression was not statistically significant ($P = .07$) in the composite endpoint analysis; however, this subgroup was small (**Table 4**).

Sensitivity Analyses

When depression was used as a continuous outcome variable and a linear regression run separately for each depression scale

Table 2—Number (n) and percentage (%) of men with depression by category of sleep characteristic, demographic or lifestyle factor and comorbidity.

	Number of Participants in Strata	Men with Depressive Symptoms, n (%)	Pearson Chi-Square	*P* Value
OSA				
No	375	43 (11.5)	6.4	.041
Mild–moderate	319	48 (15.0)		
Severe	94	20 (21.3)		
Excessive daytime sleepiness				
No	687	84 (12.2)	15.3	< .001
Yes	101	27 (26.7)		
Sleep time with O_2 saturation < 90%				
< 4% of time	600	85 (14.2)	0.01	.908
≥ 4% of time	188	26 (13.8)		
Nocturnal intermittent hypoxia (ODI)				
Mild (< 5)	256	34 (13.3)	5.25	.072
Moderate (5–24.9)	435	56 (12.9)		
Severe (≥ 25)	97	21 (21.6)		
Arousal index (quartiles)				
Lowest	198	25 (12.6)	1.66	.646
2	194	24 (12.4)		
3	202	31 (15.3)		
Highest	194	31 (16.0)		
Marital status †				
No	164	33 (20.1)	6.23	.013
Yes	624	78 (12.5)		
Financial strain ‡				
No	143	35 (24.5)	15.58	< .001
Yes	645	76 (11.8)		
Current smoker				
No	658	87 (13.2)	2.46	.117
Yes	130	24 (18.5)		
Alcohol risk				
None-low	738	101 (13.7)	1.71	.190
Medium-high	49	10 (20.4)		
Cardiovascular disease including tachycardia				
No	722	100 (13.9)	0.40	.529
Yes	66	11 (16.7)		
Diabetes				
No	652	86 (13.2)	2.51	.113
Yes	136	25 (18.4)		
Joint pain				
No	682	92 (13.5)	1.49	.222
Yes	106	19 (17.9)		
Erectile dysfunction				
No	594	74 (12.5)	5.29	.021
Yes	194	37 (19.1)		

† = married or living with partner. ‡ = "I am/we are spending more money than I/we get" or "I/we have just enough money to get me/us through to the next pay day."

(CES-D or BDI-1A), we observed the same qualitative results as reported previously for the BDI-1A, but for the CES-D the interaction between OSA and EDS did not reach significance (**Figure 2**). In the CES-D covariate unadjusted analysis both elevated OSA and sleepiness were still associated with depression, but in the multivariate analyses both factors were nonsignificant, with risk being dominated by financial strain. Lower sleepiness scores were also reported in the CES-D cohort, which may explain why we did not observe an interaction between OSA and sleepiness. Regression models run with BMI instead of WC had similar results. The mean time difference between the clinical assessment and sleep study

Table 3—Multiple adjusted regression analysis of factors associated with depression.

	Unadjusted OR (95% CI)	Model 1 † Adjusted OR (95% CI)	Model 2 † Adjusted OR (95% CI)
Mild–moderate undiagnosed OSA ‡	1.37 (0.88–2.13)	1.35 (0.85–2.14)	1.32 (0.83–2.10)
Severe undiagnosed OSA §	2.09 (1.16–3.75)*	1.97 (1.04–3.71)*	1.98 (1.05–3.73)*
Excessive daytime sleepiness	2.62 (1.60–4.30)*		2.33 (1.39–3.89)*
Unmarried ††	1.76 (1.13–2.76)*	1.56 (0.98–2.47)	1.57 (0.98–2.49)*
Financial strain ¶	2.43 (1.55–3.81)*	2.25 (1.42–3.57)*	2.15 (1.35–3.44)*
Age (y)	1.00 (0.98–1.02)	0.98 (0.96–1.00)	0.98 (0.96–1.00)
Waist circumference (cm)	1.01 (0.99–1.03)	1.00 (0.98–1.02)	1.00 (0.98–1.02)
Current smoker	1.49 (0.90–2.44)	1.47 (0.87–2.49)	1.50 (0.88–2.55)
Erectile dysfunction	1.66 (1.07–2.55)*	2.09 (1.20–3.64)*	1.96 (1.12–3.42)*

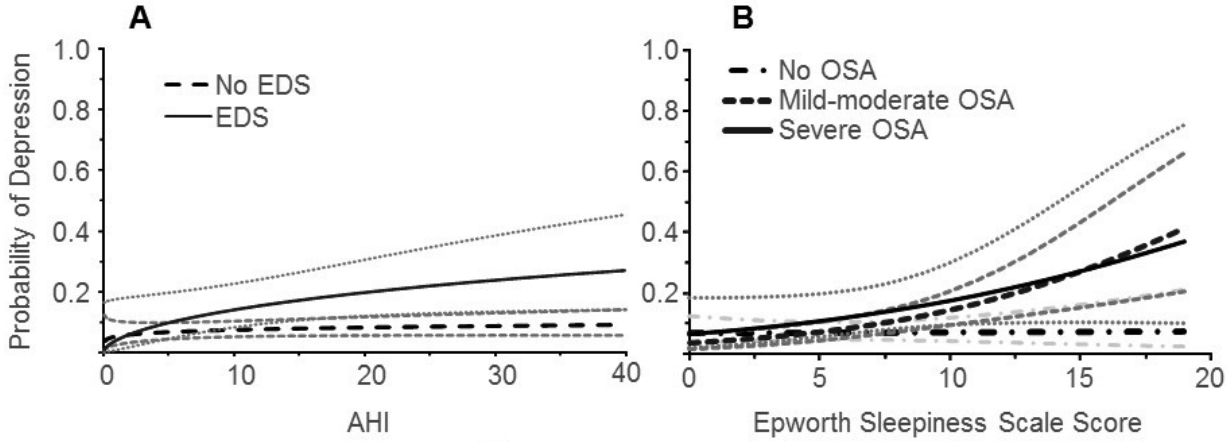
† = Model 1 adjusted for all variables listed except excessive daytime sleepiness and Model 2 adjusted for all variables listed including excessive daytime sleepiness. * = $P < .05$. ‡ = AHI 10–29 versus AHI < 10. § = AHI > 30 versus AHI < 10. †† = not currently married or living with a partner, divorced or widowed. ¶ = "I am/we are spending more money than I/we get" or "I/we have just enough money to get me/us through to the next pay day." CI = confidence interval, OR = odds ratio, OSA = obstructive sleep apnea.

Table 4—Multiple adjusted regression analysis showing the combined effect of obstructive sleep apnea and excessive daytime sleepiness on depression.

	Number of Participants in Strata	Men with Depressive Symptoms, n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI) †
No OSA + No EDS	332	37 (11.1)	1.0	1.0
No OSA + EDS	43	6 (14.0)	1.29 (0.51, 3.27)	1.19 (0.47,3.05)
Mild–moderate OSA + No EDS	274	32 (11.7)	1.05 (0.64, 1.74)	1.04 (0.62, 1.75)
Mild–moderate OSA + EDS	45	16 (35.6)	4.40 (2.19, 8.85)*	3.86 (1.87, 7.95)*
Severe OSA + No EDS	81	15 (18.5)	1.81 (0.94, 3.49)^	1.69 (0.85, 3.36)
Severe OSA + EDS	13	5 (38.5)	4.98 (1.55, 16.03)*	4.82 (1.42, 16.35)*

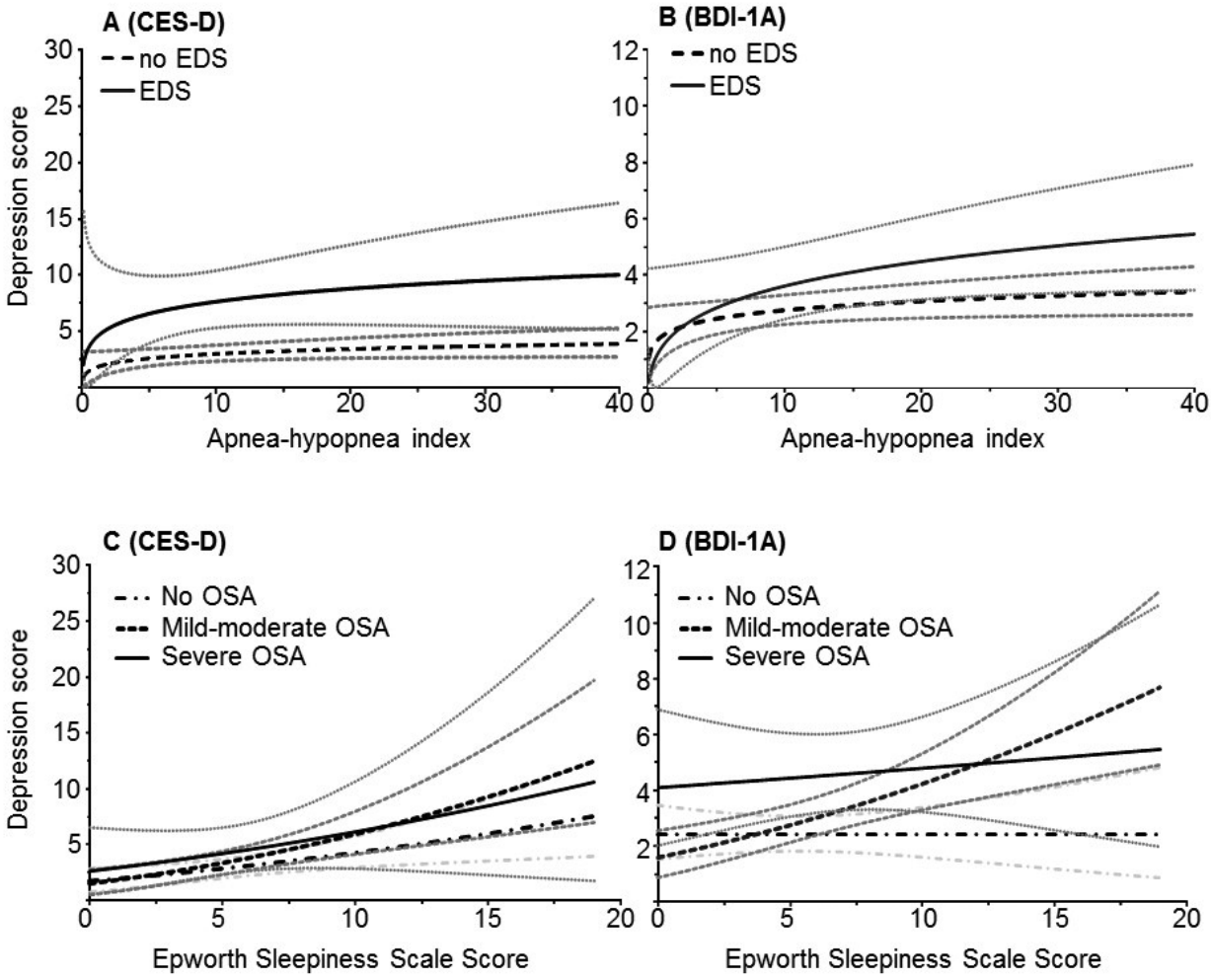
† = model adjusted for age, financial strain, marital strain, waist circumference, current smoking and erectile dysfunction. * = $P < .05$. ^ = $P = .07$. Mild–moderate OSA = AHI 10–29. Severe OSA = AHI > 30. No OSA = AHI < 10. 95% CI = 95% confidence interval, EDS = excessive daytime sleepiness, OR = odds ratio, OSA = obstructive sleep apnea.

Figure 1—Predicted probability of depression in the fully adjusted regression* for **(A)** AHI with or without EDS and **(B)** Epworth Sleepiness Scale scores with differing OSA severities.



*Presented probabilities are for a non-smoking, married man with median age (59 years) and waist circumference (99.3 cm), not experiencing financial strain or erectile dysfunction. Black lines represent estimated probability of depression for no EDS (dashed black line), EDS (solid black line) in Figure 1A. Black lines represent estimated probability of depression for no OSA (dash-dot-dash-patterned black line), mild–moderate OSA (dashed black line) and severe OSA (solid black line) in Figure 1B. Gray lines represent the standard errors as follows: Figure 1A = no EDS (square dot-patterned gray lines), EDS (round dot-patterned gray lines); Figure 1B = no OSA (dash-dot-dash-patterned gray lines), mild–moderate OSA (square dot-patterned gray lines), severe OSA (round dot-patterned gray lines). AHI = apnea-hypopnea index, EDS = excessive daytime sleepiness, OSA = obstructive sleep apnea.

Figure 2—Mean depression scale score in the fully adjusted regression* for **(A,B)** AHI with or without EDS and **(C,D)** Epworth Sleepiness Scale scores with differing OSA severities split by type of depression questionnaire.



*Presented probabilities are for a non-smoking, married man with median age (59 years) and waist circumference (99.3 cm), not suffering from either financial strain or erectile dysfunction. Black lines represent estimated mean depression score for no EDS (dashed black line), EDS (solid black line) in Figure 2A and 2B. Black lines represent estimated mean depression score for no OSA (dash-dot-dash-patterned black line), mild–moderate OSA (dashed black line) and severe OSA (solid black line) in Figure 2C and 2D. Gray lines represent the standard errors as follows: Figure 2A and 2B = no EDS (square dot-patterned gray line), EDS (round dot-patterned gray line); Figure 2C and 2D = no OSA (dash-dot-dash-patterned gray line), mild–moderate OSA (square dot-patterned gray line), severe OSA (round dot-patterned gray line). AHI = apnea-hypopnea index, BDI-1A = Beck Depression Inventory-1A (as used in the FAMAS cohort), CES-D = Centre for Epidemiological Studies Depression Scale (as used in the NWAHS cohort), EDS = excessive daytime sleepiness.

for the participants was 2.2 ± 0.8 years, with 25% of the men undergoing their sleep study within 1.5 years of their clinical assessment. However, time between assessments (ie, time between sleep study and clinical assessments) was not associated with outcome and did not influence the strength of significance of the OSA-EDS interactions in either the linear or logistic regressions.

DISCUSSION

In our male population-based sample, undiagnosed severe OSA was associated with depression after adjustment for physical and demographic risk factors, EDS and other possible intermediary sleep variables. In men with undiagnosed OSA, the odds of also having had depressive symptoms increased with increasing severity from 1.3- to 2.0-fold between mild to moderate and severe OSA, respectively. Our data indicates an interaction between OSA and EDS that is additive in terms of increasing the associations we observe between OSA, EDS, and depression. The interaction was particularly apparent in the group with mild–moderate OSA, resulting in a significant association with depression only when men had both mild–moderate OSA and EDS.

In contrast to the Wisconsin Sleep Cohort Study,[9] we found a significant interaction between OSA severity and sleepiness in the relationship with depression. EDS is considered a cardinal symptom of OSA and is also known to be associated with depression.[23,24] Due to the effect on daytime functioning, EDS is likely to be a factor in self-referral to a general practitioner

and general practitioner referral to a sleep clinic[25] and thus, contributes to OSA diagnosis. Given our study cohort consisted of men who did not have a previous OSA diagnosis, we speculate that these men may be less likely to also report EDS because they have not been sufficiently affected by sleepiness in their daily tasks to seek treatment previously. Only 13% of all of our male participants were classified as excessively sleepy using the Epworth Sleepiness Scale, which is consistent with population estimates from recent international literature[7] but considerably less than the 40% to 58% in patients referred to sleep clinics.[23] Sleepiness does not correlate well with OSA severity[24] and in our study the percentage of men with excessive sleepiness remained similar irrespective of the presence or severity of undiagnosed OSA. However, in the current study, the men with undiagnosed OSA and EDS have the highest likelihood of having depressive symptoms, in comparison with those with either condition alone. This observation is consistent with that in patients with suspected OSA reporting to an otolaryngology clinic.[24] Sleepiness that persists after successful treatment of OSA with continuous positive airway pressure therapy has been associated with persistent depressive symptoms.[14] A study of surgical treatment of OSA found that it was reduction in sleepiness scores, and not OSA severity, that was predictive of improvement in depression scores.[24] In a sleep clinic setting, this suggests that it is those patients with OSA of any severity and EDS who may benefit most effectively from depression screening. In the community setting, innovative screening or health promotion strategies will be required to identify men with undiagnosed OSA before depression screening can also be undertaken. However, men known to practitioners to have depressive symptoms might also benefit from OSA screening, particularly if they also report daytime sleepiness. Further work needs to be done on whether adding depressive symptoms to screening tools for OSA can improve identification of men with severe OSA.

Our study design does not enable us to draw causal inferences as to the direction of the association we observed between undiagnosed severe OSA and depression. The Wisconsin Sleep Cohort Study[9] reported that a diagnosis of OSA increases the odds of the development of incident depression by 1.8-fold, which supports a directional relationship whereby OSA predicts depression development. Sleep fragmentation and intermittent nocturnal hypoxia have been suggested as mechanisms through which OSA may contribute to depression in patients with OSA.[26] Oxygen saturation, intermittent hypoxia, and the arousal index were not associated with depression in the current study. It is possible that more severe intermittent hypoxia episodes, assessed by desaturations at 4%, may be more strongly associated with depression. Other physiological mechanisms through which OSA and depression may interact with each other in either direction include common inflammatory, nitric oxide signaling, noradrenergic, and dopamine pathways.[27,28]

The strengths of this study include a focus on objectively measured undiagnosed OSA, the representative community-based sample of men and the number of participants. Although the time difference between clinical assessments and the sleep study may be a study limitation, our sensitivity analysis provided no evidence that this difference influenced our results. Other limitations include the lack of an objective measure of limb movement, possible bias due to self-report measures, and the use of two different depression questionnaires. Strengths of the CES-D and BDI-1A depression scales include a high correlation with clinical evaluation of patients and their reliability and validity, even in OSA populations.[9,29,30] However, our sensitivity analyses demonstrate that the association we report in this article is present in only one of the two smaller community cohorts when analyzed independently. We did account for antidepressant use at the time of the sleep study in order to minimize the misclassification of individuals with medically controlled depression as not depressed. Future assessments will include a follow-up depression questionnaire in these participants, allowing us to report if an association between OSA and depression incidence exists longitudinally in this population. Finally, as our findings are only generalizable to men, future studies examining this issue in women are needed.

In summary, we found that severe undiagnosed OSA and EDS were both associated with depression. Our findings suggest that the odds of having clinically significant depression are highest in men with both OSA and EDS, who make up 2.0% of the men in our study population. A much larger group of men (11%) who have severe apnea without EDS still have almost two-fold increased odds for depression. It is important that clinicians and primary care practitioners consider screening for depression in men with severe OSA and for OSA in men with depression. Screening for depression should also be considered in men with EDS regardless of OSA severity.

ABBREVIATIONS

95% CI, 95 percent confidence interval
AHI, apnea-hypopnea index
BDI-1A, Beck Depression Inventory-1A
BMI, body mass index
CATI, computer-assisted telephone interview
CES-D, Centre for Epidemiological Studies Depression Scale
EDS, excessive daytime sleepiness
FAMAS, Florey Adelaide Male Ageing Study
MAILES, Men Androgen Inflammation Lifestyle Environment and Stress Study
NWAHS, North West Adelaide Health Study
ODI, oxygen desaturation index
OR, odds ratio
OSA, obstructive sleep apnea
WC, waist circumference

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