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SCIENTIFIC INVESTIGATIONS

# The Prevalence of Depression among Untreated Obstructive Sleep Apnea Patients Using a Standardized Psychiatric Interview

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**Study Objectives:** The aims of this study were: (1) to use a standardized psychiatric interview, conducted by a trained psychologist to assess the prevalence of depression among patients with untreated OSA, and (2) to identify if OSA severity or other comorbid disorders (insomnia, hypertension, and diabetes) are related to depression among patients with untreated OSA.

**Methods:** Participants were newly diagnosed patients with OSA (n = 284) waiting to start positive airway pressure (PAP) treatment. The Mini International Neuropsychiatric Interview (MINI) was used to assess depression.

**Results:** Overall, 15.5% of the sample met the diagnosis for dysthymia. Women had a significantly higher prevalence (29.5% versus 11.7% among men, p < 0.001). The prevalence of major depression was 6% in the overall sample and there was no difference in the prevalence among sexes (5.8% among men versus 6.6 % among women). Obesity, daytime sleepiness, low physical activity, initial and late insomnia, low quality of life, and sleep medication and antidepressant use were all related to depression, whereas OSA severity, as measured by apnea-hypopnea index or oxygen desaturation index, was not. Daytime sleepiness, initial insomnia, and sleep medication use were the strongest predictors of depression in multivariable analyses.

**Conclusions:** Sleep medication use, daytime sleepiness, and symptoms of initial insomnia were independently related to depression but OSA severity was not. Increased awareness of the relationship between depression and OSA and the appropriate use of assessment tools might substantially improve diagnostic accuracy as well as treatment outcome for both disorders.

**Keywords:** depression, obstructive sleep apnea, psychiatric interview

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## INTRODUCTION

Obstructive sleep apnea (OSA) is a disorder characterized by loud snoring and recurrent apneas and hypopneas during sleep, associated with oxygen desaturation and arousals.[1] Fragmented sleep and poor sleep quality are common among patients with OSA and often result in decreased energy, excessive sleepiness, impaired cognition, and altered mood.[2] This disrupted sleep pattern affects the stress system of the body and makes those suffering from OSA more vulnerable to depression.[3]

Prevalence studies have shown high rates of depression among patients with OSA in both community and clinical populations, ranging from 7% to 63%.[4–6] Furthermore, several studies have shown that patients with OSA and high levels of depression have the lowest quality of life and suffer most from daytime sleepiness and fatigue.[7–9] It has also been suggested that, among patients with OSA and depression, daytime sleepiness is more strongly related to depression than OSA severity.[8–10] Daytime sleepiness has also been shown to be more related to depression than other OSA symptoms in a general population sample.[11]

In addition to daytime sleepiness and fatigue, the high comorbidity of insomnia among patients with OSA reported in our previous studies[12,13] could also partially explain elevated levels of depression among this population, as epidemiological studies have reported that individuals with insomnia have nearly four times higher risk for the development of a new depressive disorder in the 3.5 y following insomnia diagnosis.[14]

Although depression seems to play a role in the overall expression of OSA, the true nature of this relationship remains

**BRIEF SUMMARY**

**Current Knowledge/Study Rationale:** Most previous studies have used self-reported questionnaires to assess depression among OSA patients and as a result, overrepresentation of the prevalence is likely to occur due to the frequent symptom overlap between depression and OSA. As a result, it is unclear if OSA and depression express a real comorbidity or only share similar symptoms.

**Study Impact:** In this study, the prevalence of depression in a sample of patients with untreated OSA assessed with a standardized clinical psychiatric interview is lower than reported in previous studies. Increased awareness of the relationship between depression and OSA and the appropriate use of assessment tools might significantly improve diagnostic accuracy as well as treatment outcome for both depression and OSA.

uncertain. Previous studies on OSA and mental health have focused on the level of depression in the OSA population. Symptoms such as fatigue, loss of interest, decreased libido, and poor concentration are common to both depression and OSA, which means that commonly used depression scales may not be valid in assessing depressive symptoms among patients with OSA.[6] Most standardized self-report questionnaires used to evaluate depression among patients with OSA have not been specifically designed for assessment in this population[15] and may therefore have problems in their application in this population. As a result, it is unclear if OSA and depression express a real comorbidity or only share similar symptoms.[16]

Because of the frequent symptom overlap between depression and OSA, it is important to carefully select the instruments used to measure depression in this population. In order to do so, the aims of the current study were: (1) to use a standardized psychiatric interview, conducted by a trained psychologist to assess the prevalence of depression among untreated patients with OSA, and (2) to identify whether OSA severity or other comorbid disorders (insomnia, hypertension, and diabetes) are related to depression among patients with untreated OSA.

## METHODS

Participants in this study were 284 patients in whom OSA had been diagnosed in Iceland and referred for positive airway pressure (PAP) treatment to the Landspitali-The National University Hospital in Iceland from February 2010–December 2013. A total of 104 of the 284 participants were also taking part in an ongoing study of the relationship between OSA and cardiovascular diseases and response to PAP treatment in lean and obese patients. Subjects who had been excluded from the aforementioned study were invited to take part in the current study with no inclusion/exclusion criteria other than having an apnea-hypopnea index (AHI) ≥ 15 (n = 180). All 284 subjects in the current study went through the same protocol for data collection.

All participants had received an initial diagnosis of OSA as defined by AHI ≥ 15 events/h and oxygen desaturation index (ODI) ≥ 10 events/h. When sleep studies were rescored, there were however some subjects (n = 9) who had AHI between 10–15 events/h but they were not excluded from the study. More than 90% of approached subjects agreed to participate in the study. The study protocol was approved by the National Bioethics Committee of Iceland and the Data Protection Authority of Iceland (10-048).

### General Health Questionnaire

Participants were invited to the outpatient clinic at the Landspitali University Hospital in Reykjavik, Iceland before initiating OSA treatment. After written informed consent was obtained, they answered self-administered standardized questionnaires about their current sleep-wake problems and health condition and underwent a standardized psychiatric diagnostic interview. The general health questionnaire included questions about whether subjects had hypertension and/or diabetes (medical diagnosis and medication). Women were asked if they were postmenopausal and all patients were asked if they exercised on a regular basis (yes/no). Furthermore, subjects were asked to list all medication they were taking, which were subsequently coded according to the Anatomical Therapeutic Chemical (ATC) drug classification system (www.whocc.no/atcddd). Those who listed medications in the ATC code N05C were registered as using sleep medications and those who listed medications in the ATC code N06 were registered as using antidepressants.

### Depression

Depression was evaluated with the Mini International Neuropsychiatric Interview (MINI), a short and structured diagnostic interview that contains 120 questions and screens 17 Axis I disorders according to the Diagnostic and Statistical Manual (DSM) IV criteria for 24 current and lifetime diagnosis.[17] A trained psychologist with experience in working with patients with OSA and training in administrating the MINI conducted all the interviews. Only depressive disorders (major depression and dysthymia; part A and B from the MINI) were investigated in this study.

Studies have shown that the MINI provides a reliable DSM III-R diagnosis within a short time frame.[18] For the English version of the MINI, excellent interrater and test-retest reliability, and moderate validity of MINI versus the World Health Organization Composite International Diagnostic Interview (CIDI) have been reported.[18] The Icelandic version of the MINI has not been extensively studied but one preliminary study supports its validity.[19]

A diagnosis of dysthymia according to the DSM-IV includes depressed mood for most of the day for 2 y or more and at least two of the following symptoms causing distress in life or interfering with functional ability: poor appetite or overeating, sleep problems, tiredness or lack of energy, low self-esteem, hopelessness, poor concentration, and trouble making decisions. A diagnosis of major depression includes having five or more of the following symptoms over a 2-w period, most of the day, nearly every day: depressed mood, such as feeling sad, empty, or tearful; substantially diminished interest or feeling no pleasure in almost all activities; substantial weight loss when not dieting, weight gain, or decrease or increase in appetite; insomnia or increased desire to sleep; restlessness or slowed behavior that can be observed by others; fatigue or loss of energy, feelings of worthlessness, or excessive guilt; trouble making decisions, or trouble thinking or concentrating; recurrent thoughts of death or suicide; or a suicide attempt. At least one of the symptoms must be either a depressed mood or a loss of interest or pleasure. The symptoms must be severe enough to cause noticeable problems in day-to-day activities, such as work, school, social activities, or relationships with others.[20]

Participants completed the Short Form 12 (SF-12) questionnaire to assess quality of life.[21] Two summary component scores are derived from the SF-12, the physical component score (PCS) and mental component score (MCS). These scores range from zero to 100, where zero indicates the lowest life quality and 100 indicates the highest life quality.

Daytime sleepiness was evaluated using the Epworth Sleepiness Scale (ESS), a brief questionnaire that measures subjective

**Table 1**—Baseline characteristics of the study population and characteristics of OSA patients with and without depression (dysthymia or major depression).

| | All Subjects (n = 284) | Men (n = 223) | Women (n = 61) | p for Sex Difference | Subjects without Depression (n = 225) | Subjects with Depression (n = 59) | p |
|---|---|---|---|---|---|---|---|
| Age (y) | 53.9 ± 9.1 | 53.3 ± 9.2 | 56.0 ± 8.2 | **0.041** | 54.2 ± 9.0 | 52.7 ± 9.4 | 0.281 |
| BMI (kg/m$^2$) | 33.0 ± 6.0 | 32.5 ± 5.7 | 34.8 ± 6.4 | **0.006** | 32.6 ± 5.8 | 34.5 ± 6.3 | **0.023** |
| AHI (events/h) | 33.1 ± 18.3 | 34.3 ± 18.9 | 28.6 ± 15.3 | **0.036** | 33.5 ± 18.7 | 31.7 ± 16.9 | 0.527 |
| ODI (events/h) | 29.8 ± 18.1 | 30.9 ± 18.7 | 25.6 ± 15.0 | **0.049** | 29.8 ± 18.2 | 29.7 ± 18.0 | 0.956 |
| ESS | 10.3 ± 4.4 | 10.4 ± 4.3 | 9.8 ± 4.7 | 0.401 | 9.9 ± 4.5 | 11.5 ± 3.5 | **0.017** |
| ESS > 10 (%) | 50.4 | 51.6 | 45.9 | 0.433 | 47.6 | 61.0 | 0.066 |
| Hypertension (%) | 59.4 | 57.2 | 67.2 | 0.159 | 58.0 | 64.4 | 0.375 |
| Diabetes (%) | 9.2 | 9.1 | 9.8 | 0.851 | 9.0 | 10.2 | 0.777 |
| Exercise (%) | 61.7 | 62.1 | 60.5 | 0.862 | 66.1 | 50 | 0.047 |
| Initial insomnia (%) | 18.5 | 13.6 | 36.1 | **< 0.001** | 13.5 | 37.3 | **< 0.001** |
| Middle insomnia (%) | 55.5 | 50.0 | 75.4 | **< 0.001** | 53.6 | 62.7 | 0.211 |
| Late insomnia (%) | 28.0 | 26.7 | 32.8 | 0.348 | 24.2 | 42.4 | **< 0.001** |
| Sleep medication (%) | 15.1 | 10.3 | 32.8 | **< 0.001** | 8.9 | 39.0 | **< 0.001** |
| Antidepressant use (%) | 18.3 | 15.7 | 27.9 | **0.029** | 12.4 | 40.7 | **< 0.001** |

Significance ($p < 0.05$) is marked as bold. AHI, apnea-hypopnea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; ODI, oxygen desaturation index; MCS, mental component score from the SF-12; PCS, physical component score from the SF-12.

daytime sleepiness.[22] Participants with ESS score ≥ 10 were considered to have excessive daytime sleepiness.

Sleep symptoms were assessed using the Basic Nordic Sleep Questionnaire, which includes questions on sleep quality, insomnia symptoms, snoring, nocturnal sweating, and daytime sleepiness.[23] Three subtypes of insomnia symptoms were defined: difficulty initiating sleep (initial insomnia), difficulty maintaining sleep (middle insomnia), and early morning awakenings (late insomnia), more details are outlined in an earlier study.[13] Answers were rated on a five-point scale: never/almost never (1); less than once a week (2); once or twice a week (3); three to five times a week (4); every day or almost every day of the week (5). Those who reported symptoms of insomnia at least three times per week were considered to be suffering from the appropriate subtype of insomnia.

### Sleep Apnea

All participants had a diagnostic sleep study with an Embletta type 3 portable monitor or an Embla 12 channel system (Embla, Flaga Inc., Reykjavik, Iceland) or a T3 device (Nox Medical, Reykjavik, Iceland). The sleep recordings were scored at the Landspitali University Hospital in Reykjavik by trained sleep technologists and the studies had to have at least 4 h of a scorable oxygen saturation signal and respiration by flow or respiratory inductance plethysmography belts. The AHI was calculated as the mean number of apneas and hypopneas per hour of recording (excluding upright time). The ODI was calculated as the number of transient drops in oxygen saturation ≥ 4% per hour of recording. Additional details are provided in an earlier study.[13]

### Statistical Analyses

All statistics were calculated with STATA 12.0 for Windows (Stata Corporation, College Station, TX, USA). For bivariate analysis, the chi-square test and *t*-test were used for nominal and continuous variables, respectively. Multiple logistic regression was used to identify which risk factors had an independent association with depression. The predictive value of the different models was subsequently assessed through the use of the area under the receiver operating characteristic (ROC) curve (AUC) defined according to model predicted probabilities. The AUC estimates the probability that a randomly selected depression case has a model predicted likelihood of depression that is larger than a randomly selected non-depression control.[24] Higher AUC statistics (closer to 1.0) indicate better predictive probability. We compared the AUC statistics between models using established techniques.[24] Models were compared in a sequential fashion, beginning with a model containing sex, age, and BMI only, and adding initial insomnia, ESS, and sleep medications individually and in combination.

## RESULTS

### Study Population Characteristics

Baseline characteristics and the differences between those with and without depression are shown in **Table 1**. Among the study population, the majority were male (78%) and the mean age was 53.9 ± 9.1 y, with women being on average 2.7 y older than the men. The women were more obese but with less severe OSA as measured by AHI and ODI. Furthermore, women were more likely to report symptoms of initial and middle insomnia and to use sleep medications and antidepressants (**Table 1**).

### The Prevalence of Depression

Overall, 15.5% of the sample met the diagnosis for dysthymia. Women had a significantly higher prevalence (29.5% versus

**Table 2**—Correlation matrix of all variables entered into the multivariable model.

| | Depression | Sex | Age | BMI | ESS | Initial | AHI | ODI | Sleep Medications |
|---|---|---|---|---|---|---|---|---|---|
| Depression | 1.0000 | | | | | | | | |
| Sex | 0.1925 | 1.0000 | | | | | | | |
| Age | −0.0672 | 0.1130 | 1.0000 | | | | | | |
| BMI | 0.1285 | 0.1604 | −0.2611 | 1.0000 | | | | | |
| ESS | 0.1167 | −0.0478 | −0.1053 | 0.0766 | 1.0000 | | | | |
| Initial insomnia | 0.3578 | 0.1831 | −0.1527 | 0.2049 | −0.0743 | 1.0000 | | | |
| AHI | −0.0378 | −0.1268 | −0.0956 | 0.1746 | 0.1031 | −0.1045 | 1.0000 | | |
| ODI | −0.0017 | −0.1186 | −0.1207 | 0.2481 | 0.0874 | −0.0760 | 0.8637 | 1.0000 | |
| Sleep Medications | 0.3311 | 0.0612 | 0.0612 | 0.0020 | 0.0020 | 0.2963 | −0.1053 | −0.0721 | 1.0000 |

AHI, apnea-hypopnea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; ODI, oxygen desaturation index.

**Table 3**—Factors associated with depression among patients with untreated obstructive sleep apnea.

| | Depression (Dysthymia + Major Depression), OR (95% CI)* | p |
|---|---|---|
| Sex | 1.94 (0.89–4.20) | 0.091 |
| Age | 0.99 (0.95–1.03) | 0.491 |
| BMI | 1.00 (0.95–1.06) | 0.954 |
| ESS score | 1.13 (1.04–1.23) | **0.003** |
| Initial insomnia | 1.75 (1.37–2.25) | **< 0.0001** |
| Sleep medications | 4.07 (1.81–9.14) | **0.001** |

The association is expressed as adjusted odds ratio with a 95% confidence interval. *Adjusted for all the variables in the table. Significance ($p < 0.05$) is marked as bold. AHI, apnea-hypopnea index; BMI, body mass index; CI, confidence interval; ESS, Epworth Sleepiness Scale; OR, odds ratio.

11.7% among men, $p < 0.001$). The prevalence of major depression was 6% in the overall sample and no difference in the prevalence between sexes (5.8% among men versus 6.6 % among women). The prevalence of depression overall (dysthymia or major depression) was 20.8%. Women showed significantly higher prevalence, 36.1% versus 16.6% among men, ($p < 0.001$) but this difference was driven by the dysthymia results. Furthermore, 82% of the women (n = 50) were postmenopausal, and depression was more common among them than in premenopausal women (31.8% versus 10.3%; $p = 0.04$).

Subjects who met the diagnosis for depression (dysthymia or major depression) were more obese, sleepier, and less likely to exercise on a regular basis. In addition, they had lower mental and physical quality of life, were more likely to suffer from initial and late insomnia, but had no significant difference in the prevalence of middle insomnia (**Table 2**). Furthermore, those who met diagnosis for depression were more likely to use sleep medications and antidepressants.

## Factors Associated with Depression

**Table 2** provides a correlation matrix of all variables that were entered into the multivariable model when testing independent associations to depression.

**Table 3** shows the results of logistic regression where several variables were tested for their independent associations with depression. The significance of potential risk factors for depression was evaluated, controlling for sex, age, and BMI (Model I). Apart from the variables listed in **Table 3**, diabetes, hypertension, OSA severity (AHI and ODI), exercise, and the other subtypes of insomnia (yes/no) were tested but results were not significant. Notably, OSA severity was not independently related to depression after adjusting for sex, age, and BMI (AHI: odds ratio [OR] = 0.98, $p = 0.368$; ODI: OR = 1.01, $p = 0.468$). Analyses were also performed stratified by sex. Results did not change for men, but for women, depression was only independently related to initial insomnia (daytime sleepiness as measured by the ESS was no longer significant).

**Table 4** shows that when initial insomnia was added (Model II), AUC increased from 0.631 to 0.743 ($p = 0.002$). The adjusted OR (95% confidence interval [CI]) for initial insomnia was 1.75 (1.40–2.19). When ESS score was added (Model III), AUC increased from 0.631 to 0.683 ($p = 0.02$). The adjusted OR (95% CI) for ESS score was 1.09 (1.01–1.17). Similarly, when sleep medications were added (Model IV), AUC increases from 0.631 to 0.692. The adjusted OR (95% CI) for use of sleep medications was 5.74 (2.74–12.03). Next, models containing more than one of these risk factors were evaluated to evaluate whether each contains independent predictive value. Model V contains both initial insomnia and ESS. Compared to Model II containing only initial insomnia, the AUC increased from 0.743 to 0.773. The increase in the predictive power of the model was significant ($p = 0.04$), indicating that sleepiness as reflected in ESS score provides predictive power and even accounts for presence of initial insomnia. In contrast, when sleep medications was added to Model II to produce Model VI, the increase in AUC was smaller (from 0.743 to 0.76) and not statistically significant ($p = 0.21$). When all three risk factors were included (Model VII), the AUC was 0.789. The increase in AUC from 0.773 (Model V) to 0.789 (Model VII) was not statistically significant ($p = 0.25$). However, when compared to Model I, the set of risk factors of initial insomnia, ESS, and sleep medications taken together were robustly statistically significant ($p = 0.0001$) controlling for sex, age, and BMI. In this final model the adjusted OR (95% CI) for initial insomnia, ESS, and sleep medications were 1.75 (1.37–2.25), 1.13 (1.04–1.23), and 4.07 (1.81–9.15), respectively. See **Table 4**.

**Table 4**—Predictive value of different models assessed through the use of a receiver operation characteristic curve (area under the curve).

| | Depression (Dysthymia + Major Depression) Area Under the ROC Curve* | OR (95% CI) and p value for Additional Variables* |
|---|---|---|
| **Model I:** Sex, age, BMI | 0.631 | |
| **Model II:** Sex, age, BMI, initial insomnia | **0.743**<br>**p compared to Model I = 0.0016** | **Initial insomnia 1.75 (1.40–2.19); p < 0.0001** |
| **Model III:** Sex, age, BMI, ESS | 0.683<br>p compared to Model I = 0.0240 | **ESS 1.09 (1.01–1.17); p = 0.018** |
| **Model IV:** Sex, age, BMI, sleep medications | 0.692<br>p compared to Model I = 0.050 | **Sleep medications 5.74 (2.74–12.03); p < 0.0001** |
| **Model V:** Sex, age, BMI, initial insomnia, ESS | **0.773**<br>**p compared to Model II = 0.043** | **ESS 1.13 (1.05–2.41); p = 0.002**<br>**Initial insomnia 1.90 (1.49–2.41); p < 0.0001** |
| **Model VI:** Sex, age, BMI, initial insomnia, sleep medications | 0.760<br>p compared to Model II = 0.209 | **Initial insomnia 1.63 (1.29–2.06); p < 0.0001**<br>**Sleep medications 4.13 (1.88–9.07); p < 0.0001** |
| **Model VII:** Sex, age, BMI, initial insomnia, ESS, sleep medications | 0.789<br>p compared to Model V = 0.253<br>**p compared to Model I = 0.0001** | **Initial insomnia 1.75 (1.37–2.25); p < 0.0001**<br>**Sleep medications 4.07 (1.81–9.15); p = 0.001**<br>**ESS 1.13 (1.04–1.23); p = 0.003** |

*Adjusted for all the variables in the table. Significance is marked as bold. BMI, body mass index; CI, confidence interval; ESS, Epworth Sleepiness Scale; OR, odds ratio; ROC, receiver operating characteristic.



## DISCUSSION

The main findings of the current study were that 20.8% of a sample of patients with untreated OSA met the diagnosis for depression (dysthymia or major depression) according to a structured diagnostic interview carried out by a trained psychologist. Dysthymia was more common, with 15.5% of the sample fulfilling the diagnosis. The prevalence of major depression in this study was 6%, which is similar as population studies in Europe and the United States have shown.[25,26]

In the current study, 18.3% of subjects used antidepressants and, as expected, this was more common among those who met the diagnosis for depression according to the MINI. Similar to previous findings, depression was more common among women,[6,9] but 82% of the women in the current study were postmenopausal and studies have shown a higher prevalence of depression in postmenopausal women.[27] There were very few women in our study (n = 61), and therefore, even though the difference in the prevalence of depression was quite large, it was merely significant (p = 0.04). This difference in the prevalence of depression between premenopausal and postmenopausal women needs to be studied further in studies with a larger sample of women with OSA. Controlling for age, sex, and BMI, sleep medication use, symptoms of initial insomnia, and daytime sleepiness were highly related to depression whereas OSA severity was not.

Many previous studies have found a much higher prevalence of depression among patients with OSA than reported in the current study. In a study by Mosko et al.,[28] 58% of patients with OSA met the DSM criteria for depression, and in a study by Millman et al.,[29] 45% of patients with OSA had depressive symptoms. Akashiba et al.[7] reported a 48% prevalence of depression in a sample of 60 male patients with OSA compared to controls (n = 34). In their study, patients with OSA had a much higher prevalence of depression than controls and depression was associated with poorer quality of life as we also found in our study. Furthermore, Aikens and Mendelson[30] showed that 32% of their patients with OSA had elevated depression scores on the Minnesota Multiphasic Personality Inventory (MMPI) and there were twice as many patients with OSA with elevated depression scores than age- and sex-matched primary snorers. These differences in prevalence of depression among patients with OSA are probably partially due to different definitions and instruments used to assess depression. Furthermore, the definition of OSA is important in this context. In the study by Akashiba et al.,[7] OSA was diagnosed with AHI > 20 and accompanied by daytime sleepiness, which may explain the higher depression prevalence presented in their study because daytime sleepiness seems to influence the prevalence of depression. Not all patients referred for treatment of OSA are excessively sleepy. We have identified these distinct clusters of patients with OSA, which suggests that identifying clusters based on both symptoms and comorbidities can more fully capture the spectrum of OSA rather than relying on the severity of the disease as measured by AHI and ODI.[31]

The relationship between depression and daytime sleepiness is bidirectional because depression can also be a risk factor for excessive daytime sleepiness,[11] which further supports the need of evaluating mental health among sleepy subjects with OSA. Furthermore, there is a strong association of obesity and daytime sleepiness, regardless of OSA,[11] which suggests a need for a broader focus on interventions aimed at improving mental health and supporting weight loss among patients with OSA as well as pointing out the importance of assessing depression and obesity among sleepy subjects without OSA.

When interpreting the results it is also important to take into consideration that the Icelandic population is rather homogeneous, for example, regarding ethnic background and socioeconomic status, although in the past decade or so Iceland has become more multicultural.

Most previous studies have used self-reported questionnaires to assess depression and as a result, overrepresentation of the prevalence is likely to occur due to the frequent symptom overlap between depression and OSA. An Australian study by Douglas et al.[32] showed that among patients with suspected OSA, the overall rate of depression based on doctor diagnosis, Hospital Anxiety and Depression Scale (HADS), or two screening questions from the MINI was 53%. In that study, the prevalence of depression assessed with the MINI questions was 45% and a significant correlation was reported (0.736; $p < 0.001$) between HADS and the MINI depression questions.[32] This is a much higher prevalence of depression than reported in our study but the fact that Douglas et al.[32] only used two screening questions from the MINI has to be considered a limitation and could partially explain the difference in the results. Another recent study indicated that HADS would be an accurate screening tool for assessing major depression among patients in sleep disorder clinics[33] but further studies comparing the use of self-report questionnaires and structured clinical interviews in large cohorts of patients with OSA are needed.

Patients with untreated OSA have a very high prevalence of insomnia and daytime sleepiness and, as we report here, these factors are related to depression and need to be taken into account when treating OSA. Studies have shown that symptoms of initial insomnia tend to persist, even though OSA is successfully treated whereas middle insomnia improves with PAP treatment,[12] indicating that initial insomnia requires additional treatment apart from OSA. Our results further emphasize this point because initial insomnia is related to depression in our study and depression has been associated with lack of compliance with medical treatment.[34] Use of sleep medications is also highly associated with depression in our study. Others have indicated an association between high dosages of hypnotics, sleep related breathing disorder, and depression[35] but this needs to be studied further. Because insomnia and hypnotics use is so prevalent among patients with OSA it could be beneficial to treat initial insomnia in patients with OSA with cognitive behavioral treatment before PAP is started. Results regarding the effect of depression on PAP adherence are inconsistent,[6] but a recent study indicated that depressed patients with OSA might have poorer compliance with PAP treatment.[36]

Furthermore, a number of studies have indicated a bidirectional relationship between poor sleep and depression; some have suggested that sleep difficulties may lead to or exacerbate depression and that by improving sleep quality it is possible to improve symptoms of depression as well.[37,38] OSA severity was not related to depression in our study and others have reported similar results, suggesting that depression is more related to disrupted sleep and sleepiness than OSA severity *per se*.[9]

One limitation of the current study is that OSA was evaluated with a type 3 sleep study rather than a full polysomnography. However, the NOX T3, which is a portable respiratory sleep monitor was used for the majority of patients in the current study, has demonstrated a very good measurement agreement as compared to polysomnography.[39] Another limitation is that this is a cross-sectional study and therefore follow-up data regarding changes in depression after PAP treatment and the effect of depression on PAP adherence are missing. Another limitation is how few women were enrolled in this study but as stated previously, it is important to further study the relationship between depression and menopause in a larger sample of women with OSA.

The major strengths of the current study were the large cohort of patients with untreated OSA and the use of a standardized psychiatric interview to assess depression. The MINI includes questions regarding symptoms that are highly related to untreated OSA and therefore misdiagnosis of depression is possible. However, structured diagnostic interviews such as the MINI have become an essential part of psychiatric medicine. Apart from being the diagnostic gold standard in mental health research, the MINI is also increasingly being used to help ensure diagnostic precision in clinical practice.[40] Even though information collected from open clinical interviews may vary depending on how a particular question is asked or framed, structured diagnostic interviews include questions that are precise and carefully linked to diagnostic criteria, therefore minimizing the risk of imprecise diagnosis. It is, however, time consuming to assess all patients with standardized interviews and therefore it could be more realistic to initially screen patients with self-report questionnaires and subsequently further assess those who screen positive for depression and have difficulties in adapting to PAP treatment. Additional interventions targeted at depression might be beneficial in such cases.

In conclusion, the prevalence of depression in a sample of patients with untreated OSA assessed with a standardized clinical psychiatric interview is lower than reported in previous studies. Depression among patients with OSA was more common among women and highly related to sleep medication use, daytime sleepiness, and symptoms of initial insomnia but not related to OSA severity as measured by AHI and ODI. The lack of association of AHI severity with depression in this study indicates that the actual prevalence of major depression in patients with OSA is similar to that found in the general population, whereas the prevalence of depressive symptoms and dysthymia is much greater.

Increased awareness of the relationship between depression and OSA and the appropriate use of assessment tools might significantly improve diagnostic accuracy as well as treatment outcome for both disorders.

## ABBREVIATIONS

AHI, apnea-hypopnea index
ATC, Anatomical Therapeutic Chemical
BMI, body mass index
CI, confidence interval
CIDI, Composite International Diagnostic Interview
DSM, Diagnostic and Statistical Manual of Mental Disorders
EDS, excessive daytime sleepiness
ESS, Epworth Sleepiness Scale

HADS, Hospital Anxiety and Depression Scale
MCS, mental component score
MINI, Mini International Neuropsychiatric Interview
MMPI, Multiphasic Personality Inventory
ODI, oxygen desaturation index.
OR, odds ratio
OSA, obstructive sleep apnea
PAP, positive airway pressure
PCS, physical component score
ROC, receiver operating characteristic curve
SF-12, Short Form 12

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