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Original Article

Clinical depression in untreated obstructive sleep apnea: examining predictors and a meta-analysis of prevalence rates

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ABSTRACT

Objective/background: Patients with obstructive sleep apnea (OSA) experience daytime sleepiness, cognitive impairment and depressive symptoms. However, the measured prevalence of clinical depression in OSA using standardized clinical assessment is currently unclear. The aims of this study were to examine the prevalence of clinical depression and antidepressant use in untreated OSA patients, to examine predictors of depression, and to conduct an exploratory meta-analysis to determine the pooled prevalence of clinical depression in this population.

Patients/methods: In sum, 109 consecutive patients with diagnosed OSA (mean age (SD) = 52.6 (12.1) years; 43.1% female) who presented to the sleep laboratory completed a structured clinical interview for depression (SCID-IV), the Hospital Anxiety and Depression Scale, the Pittsburgh Sleep Quality Index (PSQI), the Functional Outcomes of Sleep Questionnaire (FOSQ), the Assessment of Quality of Life Questionnaire (AQoL) and the Epworth Sleepiness Scale (EES). An exploratory meta-analysis was also conducted to quantify the risk of clinical depression in untreated OSA.

Results: Twenty-five (22.7%) participants had clinical depression based on the SCID-IV, and 24.8% were using antidepressants. Those with clinical depression had significantly poorer sleep quality and impaired quality of life. In a regression model, quality of life impairment was most strongly associated with clinical depression. Results from the meta-analysis revealed a pooled prevalence of 23% of clinical depression in OSA patients across seven studies.

Conclusion: Clinical depression and antidepressant use is common in patients with OSA. Depression was associated with reduced quality of life and poorer subjective sleep, however it was not associated with polysomnographic measures or daytime sleepiness. Whether CPAP treatment can alleviate the burden of clinical depression needs to be determined in future studies.

1. Introduction

Obstructive sleep apnea (OSA) is a common sleep disorder, with recent prevalence estimates of 23.4% in women and 49.7% in men over 40 years [1]. The repetitive sleep disruption caused by untreated OSA has significant consequences for daytime functioning, including profound daytime sleepiness [2] and impairments in cognitive function, mood and quality of life [3–5]. One of the most significant comorbidities recognised among OSA patients is psychological symptoms such as depression and anxiety [6,7]. Antidepressant use is also prevalent among patients attending a sleep laboratory for investigation of OSA, with up to a quarter of patients using pharmacotherapy for depression [8]. OSA patients report significantly higher depressive symptoms compared to non-OSA cohorts, with prevalence estimates of between 17 and 48% [6]. This is compared to a lifetime prevalence of 3–17% worldwide [9].

Abbreviations: Beck depression inventory, BDI; diagnostic and statistical manual of mental disorders four, DSM-IV; excessive daytime sleepiness, EDS; Hamilton depression rating scale, HDRS; hospital anxiety and depression scale, HADS; major depressive disorder, MDD; obstructive sleep apnea, OSA; structured clinical interview for depression, SCID.

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Studies reporting the prevalence of depressive symptoms in OSA are limited by the use of self-reported or clinician-rated assessments. Self-report scales of depression, such as the Beck Depression Inventory II (BDI-II) [10], contain items relating to symptoms that are common to both OSA and depression (eg, fatigue, somatic symptoms, loss of interest and poor concentration) [11]. The presence of a sleep disorder and its symptoms may elevate the psychiatric scores on these scales, thus curtailing their usefulness in determining clinical depression in this population. There are a number of distinct features of clinical depression that are not seen in OSA, which can be determined with a careful clinical assessment, although few studies have taken this approach [8,12–16]. These studies have reported a prevalence of between 21.5% and 30% for a current depressive disorder, highlighting the high prevalence of depression in these patients. To date, the impact of clinical depression in individuals with OSA has not been formally quantified using standardized clinical assessments.

It is also unclear whether there are particular risk factors associated with OSA that contribute to depression in these patients. OSA and major depressive disorder (MDD) share a number of diagnostic criteria and common risk factors (eg obesity, increasing age, lower socioeconomic status, hypertension, diabetes), which may in part explain their high comorbidity. From the limited studies to date, daytime sleepiness, insomnia and use of sleeping medication appear to be significant predictors of depression, whereas OSA severity measures correlate poorly [12,13,17]. Thus, it is unclear whether OSA and depression are distinct comorbidities or simply share overlapping symptoms.

The aims of the current study were (1) to examine the prevalence of clinical depression, as assessed by a structured clinical interview conducted by a trained psychologist, and antidepressant use in patients with untreated OSA; (2) to determine whether sleep, health or demographic factors predict clinical depression; and (3) conduct an exploratory meta-analysis of studies that have used structured clinical interviews for depression in OSA samples to quantify the magnitude of this effect.

2. Materials and methods

2.1. Participants

We report here the baseline data collected within the CPAP for OSA and Depression (COSAD) trial. COSAD is a randomised controlled trial (trial registration: ACTRN12614000013662) conducted at Austin Health Institute for Breathing and Sleep, approved by the Austin Health Human Research Ethics Committee. The study recruited patients aged over 18 years who had been diagnosed with OSA and recommended for CPAP treatment. Potential participants were also required to be fluent in English with no likelihood of pregnancy.

Participants were excluded if there was: a history of or current psychiatric or unstable medical condition (except depression) including epilepsy, recent stroke, myocardial infarction (in last six months); excessive daytime sleepiness (ESS>16, for safety reasons); head injury with loss of consciousness >15 min; learning disability; alcohol or drug dependence; shiftwork; and any neurological disorder or inability to complete the trial in the judgment of the clinician investigator. Participants completed demographics, medical and sleep questionnaires at their consent session, and underwent a clinical interview for depression at their first study visit.

2.2. Measures

Clinical depression was evaluated using the Structured Clinical Interview for Depression (SCID-IV) [18], which is the gold standard for assessing mood disorders according to the Diagnostic and Statistical Manual of Mental Disorders [19]. This research version may be cropped to include only the disorders that the researchers wish to target. Modules A, D, and J were used (Mood Episodes, Mood Disorders, and Minor Depressive Disorder), taking approximately 30 min to administer. The Non-Patient edition was employed as it is designed for use in non-psychiatric populations and was administered by a trained research assistant under the supervision of a registered psychologist.

Subjective sleep was assessed using the Epworth Sleepiness Scale (ESS [20]), the Pittsburgh Sleep Quality Index (PSQI [21]). Depressive symptoms, anxiety and stress were assessed using the Depression Anxiety Stress Scale (DASS-42 [22]) and the Hospital Anxiety and Depression Scale (HADS [23]) and quality of life was assessed with the Functional Outcomes of Sleep Questionnaire (FOSQ [24]) and The Assessment of Quality of Life Questionnaire (AQoL8 [25]). The AQoL-8D provides information on the following dimensions: Independent Living; Relationships; Mental Health; Coping; Pain; Senses; Self-worth and Happiness, and the super dimensions Physical (independent living, senses, pain) and Mental (relationships, mental health, coping, self-worth and happiness). Health Utility scores were also derived [26].

2.3. Meta-analysis

An exploratory meta-analysis was conducted according to the Preferred. Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines to quantify the risk of clinical depression in untreated OSA.

2.3.1. Search strategy

A systematic review of the literature was conducted to search for papers that used clinician-diagnosed depression via clinical interview in sleep clinic patients, using PsycINFO and PubMed database searches from January 1, 1995 to August 1, 2018. The search terms used were [(depression) OR (clinical depression) OR (major depressive disorder) OR (major depression)] AND (obstructive sleep apnoea). Articles were limited to peer review, human subjects, and articles written or translated in English. In addition, ancestry approach was utilised to search for other relevant articles.

2.3.2. Identification and selection of studies

A total of 1118 articles were identified from the initial search. Titles and abstracts were screened by MLJ and PV for relevancy. Articles were excluded if they: (1) did not investigate OSA or depression; (2) investigated sleep conditions other than OSA; (3) investigated medical conditions other than OSA; (4) investigated treatment/intervention for other medical conditions; and (5) were reviews, case studies or theoretical articles. 56 articles satisfied the primary inclusion criteria and were accepted for full review.

Full text was examined for remaining articles to ensure they contained original data and were relevant to the research question (ie prevalence of clinical depression in OSA patients from a sleep clinic). Following eligibility criteria was used: (1) participants recruited from a sleep clinic and screened for depression (ie, not from a depression clinic and screened for OSA); (2) depression was determined via clinical interview by a clinician, and not via self-report questionnaire; and (3) did not select participants from a community sample. Fig. 1 provides flow diagram of the study selection.

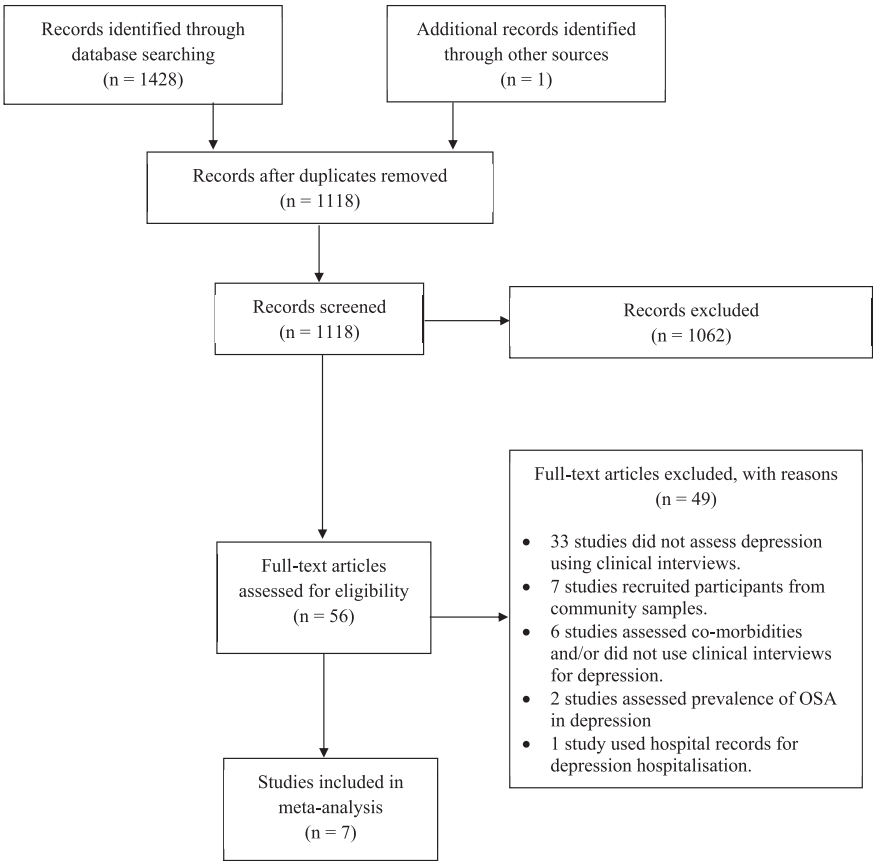

Fig. 1. Flow diagram of study selection. After assessing 1118 records, seven studies addressing prevalence of clinical depression in OSA were included in the final analysis.

2.4. Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics software version 25. Gender differences were examined using independent samples t-tests. Participants were categorized as presence or absence of current clinical depression based on the SCID-IV. Between groups comparisons were performed for depressed and non-depressed groups using independent samples *t* tests and chi^2 statistics for demographic factors, sleep, mood and quality of life measures. The analyses were repeated comparing those using and not using antidepressant medication. Logistic regression analysis was performed for the SCID-IV to examine which variables best predicted a clinical diagnosis of depression (major depression or dysthymia). Each predictor variable was run by itself initially, and those meeting the criterion of $p < 0.1$ were entered into a backwards regression model. For the meta-analysis, prevalence estimates of depression were calculated by pooling data from individual studies using random-effects meta-analysis to account for between-study heterogeneity. All analyses were performed using MetaXL [27].

3. Results

A total of 125 participants were recruited in this phase of the trial. Of these, 16 did not complete the SCID-IV, leaving 109 in this analysis (mean, SD age = 52.6, 12.1 years; 43.1% female). Because the scoring rules in our clinical Sleep Laboratory changed during the trial, the respiratory events for 58 participants were scored using AASM v1.0 criteria [28], and 44 were scored using the v2.2 criteria [29] (N = 7 unknown). To make the data equivalent, each participant's AHI was grouped into three categories (5–14, 15–29 and > 30) based on Duce et al. (2015). Demographics of the whole sample are displayed in Table 1. Antidepressant use was seen in 26.7% of the group. Women were older, had a higher BMI, reported more depressive symptoms (HADS-D), had a poorer quality of life (FOSQ) and were more likely to be using antidepressants than men (all $p < 0.05$).

3.1. Group comparisons based on depression status (SCID-IV) and antidepressant use

Twenty-five (22.9%) participants had clinical depression as determined by the SCID-IV (including dysthymia and major depression). Based on a HADS-D cut off of 8 or more [8], 26.6% of 92 participants who completed this questionnaire were considered at high risk for depression. Demographic data for depressed and non-depressed groups are presented in Table 3. Participants with depression reported significantly lower quality of life, sleep disturbance, depressive, anxiety and stress symptoms. The groups did not differ on any PSG measures; in particular, those with a higher AHI were not more likely to be depressed based on the SCID. From the PSQI subscales, participants with clinical depression reported significantly worse sleep quality ($p < 0.05$) and greater daytime dysfunction ($p < 0.05$) compared to the non-depressed group. From the FOSQ subscales, the depressed group reported significantly lower general productivity, social outcome and activity levels compared to the non-depressed group (all $p < 0.05$).

Table 2 presents the results of the AQoL subscales. Participants with clinical depression scored significantly lower on the dimensions of Independent Living ($p = 0.02$), Pain ($p = 0.003$), Mental Health ($p < 0.001$), Happiness ($p < 0.001$), Self-Worth ($p < 0.001$), Coping ($p < 0.001$), and Relationships ($p < 0.001$).

Table 1
Participant demographics, mood sleep and medication use.

N	109
Age (years)	49.4 (11.7)
Gender (males)	62 (56.9%)
BMI[b]	35.9 (9.4)
Current MDE	25 (22.9)
Past MDE[d]	55 (50.5%)
Sleep and mood scales	
ESS[f]	8.5 (3.8)
AQol[a]	85.1 (18.0)
PSQI[c]	8.8 (3.8)
FOSQ[a]	14.6 (3.5)
HADS-D[e]	5.9 (4.1)
DASS D[b]	10.0 (7.3)
DASS A[b]	11.5 (8.5)
DASS S[b]	9.2 (7.5)
Sleep variables	
AHI 5-14	14 (13.2%)
AHI 15-29	21 (19.8%)
AHI >30	71 (67.0%)
ODI 4%	17.7 (17.8)
%REM sleep[e]	16.9 (8.5)
Medication use	
Antidepressant	23 (21.1%)
Bipolar	3 (2.8%)
Anxiety	1 (0.9%)
Hypertension	37 (33.9%)
Type 2 diabetes	14 (12.8%)
Cholesterol	15 (13.8%)
Sleep medication in last month	28 (26.7%)

Note: Data indicates Mean (SD) or N (%).
AHI = apnea hypopnea index; AQoL = Assessment of Quality of Life Scale; BMI = body mass index; DASS = Depression, Anxiety and Stress Scale; ESS = Epworth sleepiness scale; FOSQ = Functional Outcomes of Sleep Questionnaire; HADS-D = Hospital Anxiety and Depression Scale depression subscale; MDE = major depressive episode; ODI4% = oxygen desaturation index <4%; %REM sleep = percentage of rapid eye movement sleep; PSQI = Pittsburgh Sleep Quality Index.
[a] *N* = 105.
[b] *N* = 104.
[c] *N* = 100.
[d] *N* = 109.
[e] *N* = 91.
[f] *N* = 108.

The clinical depression group also scored lower on the Psychological Super dimension ($p < 0.001$), and the Physical super dimension ($p = 0.009$). In terms of Health Utility scores, participants with clinical depression ($M = 0.385$) reported a significantly reduced health utility score compared to the non-depressed group ($M = 0.596$; $p < 0.001$). This is compared to Australian population norms of 0.769 for males and females aged 45–54 [30]. The minimally important difference for the Health Utility score is 0.06 [31].

Table 2
Assessment of Quality of Life subscale scores and Health utility score for the whole sample.

Dimension	Utility weighted score
Independent Living	0.80 (0.15)
Happiness	0.67 (0.16)
Mental Health	0.50 (0.08)
Coping value	0.66 (0.15)
Relationships	0.64 (0.15)
Self-Worth	0.73 (0.18)
Pain	0.65 (0.26)
Senses	0.78 (0.15)
Super Dim Physical	0.57 (0.20)
Super Dim Mental	0.26 (0.14)
Health Utility Score	0.55 (0.19)

Note: Data indicates Mean (SD).

Table 3
Participant demographics and significant differences between depressed and non-depressed groups based on the SCID-IV.

	Clinical depression	No depression
N	25 (22.7%)	85 (77.3%)
Age (years)	49.4 (11.7)	53.6 (12.1)
Gender (male)	11 (44%)	51 (60%)
BMI[c]	38.3 (9.2)	35.2 (9.4)
Past MDE[d]	11 (10.1%)	44 (40.4%)
Sleep and mood scales		
ESS[f]	9.7 (3.3)	8.1 (3.8)
AQol[a] ***	102.1 (17.0)	80.1 (12.0)
PSQI **	10.9 (3.5)	8.4 (3.8)
FOSQ[a] ***	72.5 (20.2)	88.1 (20.6)
HADS-D[e] ***	8.4 (4.2)	5.1 (3.7)
DASS D[b] ***	15.3 (7.4)	8.5 (6.5)
DASS A[b] ***	18.5 (8.1)	9.5 (7.5)
DASS S[b] ***	15.3 (7.0)	7.5 (6.8)
Sleep variables		
AHI 5–14 (%)	4 (16.7%)	10 (12.2%)
AHI 15–29 (%)	5 (20.8%)	16 (19.5%)
AHI >30 (%)	15 (62.5%)	56 (63.3%)
ODI 4%	12.2 (11.0)	19.4 (19.2)
%REM sleep	17.5 (11.1)	16.7 (7.7)
Medication use		
Antidepressant	12 (48%)	15 (18%)
Sleep medication in last month	8 (7.6%)	20 (19%)

Note: Data indicates Mean (SD) or N (%).
*** = $p \leq 0.001$; ** = $p \leq 0.01$; * = $p < 0.05$.
AHI = apnea hypopnea index; AQoL = Australian Quality of Life Scale; BMI = body mass index; DASS = Depression, Anxiety and Stress Scale; ESS = Epworth Sleepiness Scale; FOSQ = Functional Outcomes of Sleep Questionnaire; HADS-D = Hospital Anxiety and Depression Scale depression subscale; MDE = major depressive episode ODI4% = oxygen desaturation index <4%; %REM sleep = percentage of rapid eye movement sleep; PSQI = Pittsburgh Sleep Quality Index.
[a] *N* = 105.
[b] *N* = 104.
[c] *N* = 101.
[d] *N* = 109.
[e] *N* = 92.
[f] *N* = 108.

Table 4
Significant differences between participants using and not using antidepressant medication on demographic and mood variables.

	Antidepressant use	
	Yes	No
N	27 (24.8%)	82 (75.2%)
Age	54.7 (12.5)	51.9 (12.2)
Gender (males)	9 (33.3%)	53 (64.6%)
Clinical depression	12 (48%)	13 (52%)
BMI[a]	36.8 (8.4)	35.6 (9.7)
ESS[b]	9.4 (3.4)	8.2 (3.8)
AQol[c] ***	95.4 (19.9)	81.9 (16.2)
PSQI[d]	9.1 (3.9)	8.7 (3.7)
FOSQ[c] *	13.3 (3.7)	15.0 (3.3)
HADS-D[e] **	8.4 (4.7)	5.1 (3.6)
DASS D[a] *	13.2 (8.3)	10.4 (7.9)
DASS A[a] *	15.0 (9.4)	13.2 (8.3)
DASS S[a] **	13.3 (9.4)	8.0 (6.4)

Note: Data indicates Mean (SD) or N (%).
*** = $p \leq 0.001$; ** = $p < 0.005$; * = $p < 0.05$.
AQoL = Australian Quality of Life Scale; BMI = body mass index; DASS = Depression, Anxiety and Stress Scale; ESS = Epworth sleepiness scale; FOSQ = Functional Outcomes of Sleep Questionnaire; HADS-D = Hospital Anxiety and Depression Scale depression subscale; MDE = major depressive episode ODI4% = oxygen desaturation index <4%; PSQI = Pittsburgh Sleep Quality Index.
[a] N = 104.
[b] N = 106.
[c] N = 105.
[d] N = 100.
[e] N = 91.

Table 5
Logistic regression of significant predictors of depressive disorder.

Model	*B*	*S.E. B*	Wald χ^2	*p*	*OR*	95% *CI OR*
ESS	−0.071	0.102	0.493	0.483	0.93	0.76, 1.14
HADS-D	0.081	0.117	0.475	0.490	1.08	0.86, 1.36
Antidepressant use	−0.685	0.762	0.808	0.369	0.50	0.11, 2.24
Past MDE	1.185	0.742	2.676	0.102	3.27	0.79, 13.53
FOSQ	−0.187	0.140	1.796	0.180	0.83	0.63, 1.09
PSQI	0.061	0.105	0.336	0.562	1.06	0.87, 1.30
AQoL	0.075	0.032	5.391	0.020	1.08	1.01, 1.15
Constant	−6.025	3.725	2.617	0.106	0.002	

Note: Dependent variable is depressive disorder, coded 1 = presence, 0 = absence. N = 83.
HADS-D, Hospital Anxiety and Depression Scale depression score; ESS, Epworth Sleepiness Scale; MDE, major depressive episode, AQoL, Assessment of Quality of Life scale; FOSQ, Functional Outcomes of Sleep Questionnaire; PSQI, Pittsburgh Sleep Quality Index.

A separate analysis of antidepressant use, regardless of depression status, was conducted. Twenty-seven participants were currently using antidepressant medication. Table 4 displays the demographics, questionnaire scores and objective sleep measures of the two groups. Participants using antidepressants were more likely to have lower quality of life, poorer subjective sleep outcomes, and report higher depression, anxiety and stress. Of those using antidepressants, 75% had a comorbid medical condition (hypertension, type 2 diabetes, COPD or high cholesterol) or bipolar disorder.

3.2. Predictors of depression

For the SCID-IV data, multivariate logistic regressions were conducted, using presence of absence of major depression or dysthymia (Table 5). The variables that met the criterion for inclusion into the logistic regression model were ESS, AQoL, PSQI, FOSQ, HADS-D, antidepressant use and past MDE. AQoL was the only significant predictor of SCID status (Wald $\chi 2 = 15.04$, $p \leq 0.001$), predicting 40% of the variance (unstandardized [beta] = 0.10, standardised $\beta = 1.10$, CI [95%] = 1.05, 1.16).

3.3. Meta-analysis of studies reporting clinical depression in OSA samples

Seven papers, published between 1995 and 2018, met the search criteria. Including the current unpublished study, a total of 1111 participants were included (Fig. 1) [8,12–15,32]. Table 6 describes the study details. Four studies used the gold standard structured clinical interview for depression (SCID-IV), with three of these studies reporting that approximately one-third of the sample had clinical depression (29.7%–33.9%) [14,15,32]. Two studies used the Mini-International Neuropsychiatric Interview (MINI), reporting a prevalence of 20.8% [12] and 29.7% [8] of a current major depressive episode or dysthymia. Acker and colleagues conducted a psychiatric evaluation using ICD-10 criteria for major depression, reporting a prevalence of 21.5% [13]. The overall pooled prevalence of clinical depression in OSA was 0.23 (95% CI: 0.18–0.29) (Fig. 2).

4. Discussion

The current study found a prevalence of current depression of 22.7% amongst 109 unselected individuals with untreated OSA using a gold standard clinical assessment of depression. This finding is in line with previous studies that have reported a prevalence of current major depression of 29.7%–33.9% in OSA patients using the SCID-IV [14,15,32]. The prevalence was slightly overestimated using a cut-off score of <8 on the HADS-D (26.6%). Individuals with a depressive disorder in the current study reported a poorer quality of life, more sleep disturbance, higher depressive, anxiety and stress symptoms, and greater daytime dysfunction (lower general productivity, social outcome and activity levels) as a result of their sleep disorder. Similarly, those using antidepressants had lower quality of life, poorer functional outcomes of sleep, and higher stress symptoms. From the regression analyses, poor quality of life had the strongest association with both clinical depression (SCID) and depressive symptoms (HADS-D), supporting previous studies [33]. Quality of life is impacted in both OSA and depression, and therefore there is likely to be a bidirectional effect of both conditions on well-being and quality of life of the individual [34].

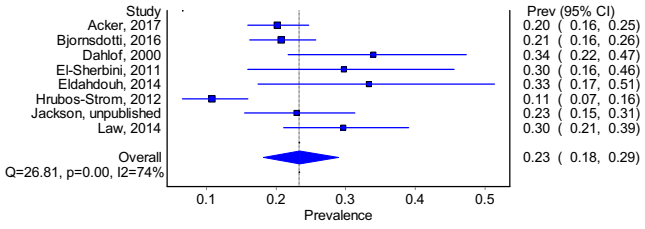

Fig. 2. Forest plot of the prevalence of clinical depression in OSA patients attending the sleep laboratory over seven published and one unpublished studies.

Table 6
Selected characteristics of cross sectional published studies included in the meta-analysis.

Study	Participants	Age (years) Mean (SD)	Depression assessment method	Prevalence of depression
Acker et al., 2017	322 OSA patients (mean AHI = 31.4), 232 males	57.6 (12.3)	Psychiatric interview using ICD-10 criteria	24.9% (26 mild, 34 moderate, 5 severe)
Bjornsdotti et al., 2016	284 OSA patients (mean AHI = 33.1), 222 males	53.9 (9.1)	Mini International Neuropsychiatric Interview	20.8% (6% major depression, 15.5% dysthymia)
Dahlof et al., 2000	53 male OSA patients (mean DI = 22.8) prior to UPPP surgery	50 (9)	Structured Clinical Interview for DSM −III−R	34% (23% major depression, 9% dysthymia, 2% DDNOS
Eldahdouh et al., 2014	30 OSA patients, 18 males	55.0 (17.6)	Structured Clinical Interview for DSM-IV	33.3% (20% mild, 13.3% moderate)
El-Sherbini et al., 2011	37 OSA patients (mean AHI = 27.7), 24 males	44.9 (8.8)	Structured Clinical Interview for DSM-IV	29.7% (7 mild, 4 moderate)
Hrubos-Strom et al., 2012	175 OSA patients	unknown	Structured Clinical Interview for DSM-IV	10.9% (16 MDD, 3 dysthymia)
Law et al., 2014	101 OSA patients (mean AHI = 14.5), 71 males	49.2 (14.5)	Mini International Neuropsychiatric Interview	29.7%

Note: AHI = apnea hypopnea index; DDNOS = depressive disorder not otherwise specified; DI = desaturation index (≥4% decrease in SaO_2) per hour of sleep; DSM = Diagnostic and Statistical Manual; ICD-10 = International Classification of Diseases 10th revision; OSA = obstructive sleep apnea; UPPP = Uvulopalatopharyngoplasty.

There were no differences in objective sleep measures or subjective daytime sleepiness between clinically depressed patients and those not meeting criteria for depression. Sleep fragmentation has been found to be the primary cause of excessive daytime sleepiness, and is suggested to be the primary driver of depressive symptoms in individuals with OSA [35]. In contrast to the current study, sleepiness and fatigue have previously been found to be associated with depressive symptoms [36,37] and clinical depression [12] in the context of OSA. It is important to note, however, that those with an ESS score >16 were excluded in our study, and as a result, the ESS mean score was below clinically significant levels (ESS >10), which may explain this discrepancy. Nonetheless, it is important to recognise that significant sleepiness may not be present in all individuals with comorbid depression and OSA.

The prevalence of antidepressant use across the whole sample was 25%, similar to previous reports [8,38]. Schwartz et al., reported that 39% of 114 consecutive patients referred to the sleep laboratory were receiving antidepressant medication at the time of referral [39]. Of these, 41% reported depressive symptoms in the mild range and 12% had moderate to severe symptoms of depression. There were also similar levels of anxiety in both groups. These data suggest that not only is antidepressant use high in sleep clinic populations, but a significant proportion of OSA patients that use antidepressants have residual depressive symptoms that are unresponsive to pharmacotherapy. These findings raise the question of the likely contribution of OSA to these residual symptoms, and whether some individuals with treatment-resistant depression may have an underlying sleep disorder. A small sub-analysis of the patients who were using antidepressants from Schwartz et al. [38], revealed that three out of nine patients had ceased using their medication after 12 months of CPAP use [38]. Thus, there is a suggestion that CPAP may alleviate the burden of clinical depression and reduce medication use, which warrants further investigation.

One of the difficulties of reporting mood symptoms in OSA samples is the gender disparity – OSA is more common in males, and depression has a higher prevalence in women. Women with OSA are five times more likely than men to have depressive symptoms, adjusting for age, BMI and OSA indices [40]. Many previous studies have a higher prevalence of men (~75–80%) compared to the current study (56.9%), and found a lower prevalence of depression as a result [12]. Our sample was also relatively young (mean age 52 years), and the prevalence of OSA [41] and depression increase with age. Even in this younger working-age sample, one in five patients had clinical depression. Therefore, the burden of depression is likely to be higher in older populations with untreated OSA.

It is also likely that other comorbid chronic diseases (including anxiety, obesity, cardiovascular disease and diabetes) may increase an individual's susceptibility to depression. This may explain why depression does not resolve in some patients after treatment of OSA. Of the participants who were being treated with antidepressants in the current study, 75% reported a comorbid medical condition (hypertension, diabetes or high cholesterol) or bipolar disorder, and a high prevalence of anxiety symptoms were also noted. The contributions of comorbid conditions, and the role of diet and exercise to assist with mental health and obesity associated with OSA, need to be further examined in future studies.

This is the first study to our knowledge that reports on the size of the effect of clinical depression in OSA patients. The overall pooled prevalence was 23% across seven published studies that used a standardized clinical interview for depression in an OSA cohort. This is significant, given that the lifetime prevalence of major depression is between 3 and 17% worldwide [9]. A point of uncertainty is the time course of depression and OSA onset. Depression, at least in some patients, may develop as a result of the sleep disorder. One observational study using a community sample of over 1400 individuals found that OSA was associated with an increased risk in the onset of depression at four-year follow-up [42]. Conversely, in some patients, the presence of depression may precipitate or exacerbate OSA through weight gain, decreased motivation for activity and exercise, alcohol use or sleep disruption. It has also been hypothesized that there are common neurobiological mechanisms underpinning the presentation of both depression and OSA, with the serotoninergic system playing a central role [43]. In others, both conditions may appear independently but the direction of this relationship is difficult as it is often unclear when OSA symptoms first manifest. Development of scales to better capture information about when symptoms commenced and the length of time an individual has experienced OSA will provide a clearer understanding of the consequences of OSA on psychological and medical conditions.

5. Conclusion

OSA is associated with high rates of clinical depression and antidepressant use. This study has demonstrated an overall prevalence of 23% of clinical depression across seven OSA studies. Depression in the context of OSA carries with it a large burden of disease, particularly reduced quality of life, as shown in this study. On the positive side, safe, effective and inexpensive treatments exist for OSA. Thus, OSA is a modifiable factor that, if treated, may reduce the economic, healthcare and personal burden of depression. Findings from the treatment phase of this study will help us determine whether clinical depression is alleviated with CPAP use, taking into account antidepressant use; whether there are subgroups of patients who respond better to treatment; and what are the characteristics of patients who respond compared to those who remain depressed. Such outcomes will greatly contribute to our knowledge of the interrelationship between these two conditions, and provide critical clinical evidence regarding the efficacy of CPAP treatment in patients with comorbid depressive disorders.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2019.03.011.

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