

# Sleep Disordered Breathing and Depression among U.S. Adults: National Health and Nutrition Examination Survey, 2005-2008

Anne G. Wheaton, PhD; Geraldine S. Perry, DrPH; Daniel P. Chapman, PhD; Janet B. Croft, PhD

*Division of Adult and Community Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA*

**Study Objective:** To determine if symptoms of sleep disordered breathing (SDB) are associated with depression symptomology in a national sample.

**Design:** National Health and Nutrition Examination Survey

**Setting:** U.S., 2005-2008.

**Participants:** 9,714 adults ( $\geq 18$  years)

**Measurements:** Respondents were asked about frequency of snoring and snorting, gasping, or stopping breathing while asleep and completed the PHQ-9 (a 9-item depression screener). Odds ratios (OR) and 95% confidence intervals (CI) for SDB symptom-associated probable major depression (defined as a PHQ-9 score  $\geq 10$ ) were obtained from sex-specific logistic regression analyses adjusted for body mass index, age, race/ethnicity, and education.

**Results:** Among men, 6.0% reported physician-diagnosed sleep apnea, 37.2% snored  $\geq 5$  nights/week, 7.1% snorted/stopped breathing  $\geq 5$  nights/week, and 5.0% had PHQ-9 scores  $\geq 10$ . Among women, 3.1% reported sleep apnea, 22.4% snored  $\geq 5$  nights/week, 4.3% snorted/stopped breathing  $\geq 5$  nights/week, and 8.4% had PHQ-9 scores  $\geq 10$ . Sleep apnea was associated with probable major depression (OR = 2.4; 95% CI: 1.5, 3.6 among men; OR = 5.2; 95% CI: 2.7, 9.9 among women). Snoring was not associated with depression symptoms in men or women. Snorting/stopping breathing  $\geq 5$  nights/week compared to never was strongly associated with probable major depression in men (OR = 3.1; 95% CI: 1.8, 5.2) and women (OR = 3.0; 95% CI: 1.6, 5.4).

**Conclusion:** Frequent snorting/stopping breathing was associated with probable major depression by the PHQ-9 in a national sample of adults. Additional research may be needed to determine whether regular screening for these conditions by mental health professionals and sleep specialists should be recommended.

**Keywords:** Sleep disordered breathing, depression, obstructive sleep apnea

**Citation:** Wheaton AG; Perry GS; Chapman DP; Croft JB. Sleep disordered breathing and depression among U.S. adults: National Health and Nutrition Examination Survey, 2005-2008. *SLEEP* 2012;35(4):461-467.

## INTRODUCTION

Sleep disordered breathing (SDB) is characterized as abnormal breathing patterns that result in sleep disturbances. SDB encompasses obstructive sleep apnea (OSA), in which partial or complete closure of the airways disrupts breathing during sleep, as well as snoring and upper airway resistance syndrome. Risk factors for OSA include being male, being older, obesity, and craniofacial morphology.<sup>1</sup> In Western countries, up to 5% of adults may have undiagnosed obstructive sleep apnea syndrome (OSA with daytime sleepiness), and up to 20% are estimated to have at least mild OSA.<sup>2,3</sup> Undiagnosed (and therefore untreated) OSA may contribute to hypertension<sup>4</sup> and other cardiovascular morbidity,<sup>5-7</sup> sleepiness,<sup>1</sup> and impaired cognitive function.<sup>8</sup>

High rates of depression (up to 63%) have often been found among patients with OSA.<sup>9-12</sup> Most investigations into the association between OSA and depression have been conducted in relatively small populations of patients diagnosed with moderate to severe OSA, but less is known about the association

between depression and the symptoms of SDB in the general, non-clinical population. Analysis of data from a large telephone survey (nearly 20,000 individuals aged 15-100 years and selected from the general population of 5 European countries) was conducted to evaluate the association between breathing-related sleep disorders and major depressive episodes.<sup>13</sup> Depressed individuals were 5 times more likely to have a DSM-IV breathing-related sleep disorder, which required the presence of insomnia, excessive daytime sleepiness, disrupted sleep, or nonrestorative sleep in addition to breathing-related symptoms, than nondepressed individuals. However, no data was presented regarding specific SDB symptoms independent of daytime sleepiness or other sleep complaints. In a study of Veterans Health Administration (VHA) patient records (approximately 4 million unique cases) from 1998 to 2001, the odds of having a depression diagnosis among patients with a sleep apnea diagnosis was nearly three times that for patients without sleep apnea.<sup>14</sup> These results may not be generalizable to the general population since veterans who use the VHA system tend to be older men and have multiple comorbidities. Using data from the Hordaland Health Study in Norway, Sivertsen et al. studied the association of self-reported OSA symptoms with long-term sick leave and work disability (7,028 subjects, aged 40-45 years).<sup>15</sup> In this study sample, the crude prevalence of depression was significantly higher among participants who reported snoring and breathing cessation in addition to daytime sleepiness, but further elaboration on this association was not included in the report since the study focused on sick leave and disability.

Submitted for publication December, 2010

Submitted in final revised form October, 2011

Accepted for publication November, 2011

Address correspondence to: Anne G. Wheaton, PhD, Division of Adult and Community Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 4770 Buford Hwy. NE, Mailstop K-67, Atlanta, GA 30341; Tel: (770) 488-5362; Fax: (770) 488-5965; E-mail: AWheaton@cdc.gov

**Table 1—Patient Health Questionnaire (PHQ-9)<sup>a</sup>**

Over the last two weeks, how often have you been bothered by the following problems (Not at all, Several days, More than half the days, Nearly every day):

1. Little interest or pleasure in doing things?
2. Feeling down, depressed, or hopeless?
3. Trouble falling or staying asleep, or sleeping too much?
4. Feeling tired or having little energy?
5. Poor appetite or overeating?
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down?
7. Trouble concentrating on things, such as reading the newspaper or watching TV?
8. Moving or speaking so slowly that other people could have noticed? (Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual?)
9. Thoughts that you would be better off dead or of hurting yourself in some way?

<sup>a</sup>The PHQ-9 questions are based on the nine Diagnostic and Statistical Manual of Mental Disorders (4<sup>th</sup> edition) signs and symptoms for depression.

As part of the Wisconsin Sleep Cohort Study, 1,408 working adults underwent polysomnography and were evaluated for depression using the Zung depression scale.<sup>16</sup> Using longitudinal models, a dose-response relationship was found between SDB severity (based on apnea-hypopnea index) and odds of developing depression ( $\geq 50$  on the Zung scale). Finally, in one small study of individuals with major depression recruited from the general population, the number of major airflow limitation events during sleep was higher in the depressed group than in non-depressed controls.<sup>17</sup>

Given the lack of literature about the possible association between SDB symptoms and depression in the general population, we used data from the National Health and Nutrition Examination Survey (NHANES) for the years 2005-2008 to assess whether the frequency of symptoms specific to SDB was associated with depressive symptomology.

## METHODS

### Study Population

Conducted annually by the National Center for Health Statistics, Centers for Disease Control and Prevention, NHANES is a stratified, multistage probability sample of the civilian non-institutionalized U.S. population. Each year, approximately 5,000 individuals are interviewed in their homes and complete the health examination components that include medical, dental, and laboratory test evaluations, usually administered in mobile examination centers. Low-income persons, persons aged  $\geq 60$  years, and non-Hispanic blacks were oversampled in both the 2005-2006 and 2007-2008 NHANES cycles. Additionally, Mexican-Americans and adolescents were oversampled in the 2005-2006 NHANES, and all Hispanics were oversampled in the 2007-2008 NHANES. For this study, adults aged  $\geq 18$  from NHANES 2005-2008 were included. NHANES was approved by the Research Ethics Review Board of the National Center for Health Statistics.

As NHANES is a public-use dataset, this study was exempt from additional review by an institutional review board.

### Sleep Disordered Breathing

The sleep disorders questionnaire was administered in the home using computer-assisted personal interviewing during the initial survey participant interview. Participants were asked 2 questions about frequency of SDB symptoms: “In the past 12 months, how often did you snore while sleeping?” and “In the past 12 months, how often did you snort, gasp, or stop breathing while asleep?” Possible responses were “never,” “rarely (1-2 nights/week),” “occasionally (3-4 nights/week),” or “frequently (5 or more nights/week).” Participants were also asked if they had ever been told they had a sleep disorder by a doctor or other health professional. If the participant’s response to this question was “Yes,” they were asked what the sleep disorder was, with sleep apnea as a possible response.

### Depression Screener

The depression screener questionnaire was administered during the computer-assisted personal interview at the mobile examination center. The series of 9 symptom questions, commonly referred to as the Patient Health Questionnaire (PHQ-9), are presented in Table 1. Each question is scored based on the frequency of the symptom over the previous 2 weeks: “0 (not at all),” “1 (several days),” “2 (more than half the days),” or “3 (nearly every day).” A total PHQ-9 score  $\geq 10$  (out of a possible 27) has a sensitivity of 88% and a specificity of 88% for major depression.<sup>18</sup> The 2 following items on the PHQ-9 may be associated with sleep in the absence of depression: “trouble falling asleep, staying asleep, or sleeping too much” and “feeling tired or having little energy.” Therefore, we also assessed a depression score based on only the first 2 items of the PHQ-9 (“little interest or pleasure in doing things” and “feeling down, depressed, or hopeless”), referred to as the PHQ-2 score. A total PHQ-2 score  $\geq 3$  (out of a possible 6) has a sensitivity of 83% and a specificity of 92% for major depression.<sup>19</sup> References to “depression” when describing respondents in this study indicate the probable presence of major depression as determined by having a PHQ-9 score  $\geq 10$  or a PHQ-2 score  $\geq 3$ . This terminology, however, does not reflect a clinical diagnosis of depression made by a health professional in a clinical setting.

### Covariates

Information was collected during the home interview component on covariates which included sex, self-reported race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican-American, other/multiracial), age category (18-24, 25-34, 35-44, 45-54, 55-64,  $\geq 65$  years), and education ( $\leq$  high school diploma, high school diploma or equivalent, some college, college graduate). Body mass index (BMI) was calculated from weight and height measured at the mobile examination center (weight [kg]/height [m]<sup>2</sup>). BMI was categorized according to the following National Heart, Lung, and Blood Institute criteria: underweight (BMI  $< 18.5$ ), normal weight ( $18.5 \leq \text{BMI} < 25$ ), overweight ( $25 \leq \text{BMI} < 30$ ), obese class I ( $30 \leq \text{BMI} < 35$ ), obese class II ( $35 \leq \text{BMI} < 40$ ), and obese class III (BMI  $\geq 40$ ).<sup>20</sup>

A total of 11,791 adults aged  $\geq 18$  years participated in the 2005-2006 and 2007-2008 NHANES cycles. Participants who

responded “refused” to the questions regarding snoring or snorting/stopping breathing were excluded ( $n = 4$ ). Of the remaining number, 461 did not participate in further examinations at the mobile examination centers. From the resulting eligible population ( $n = 11,326$ ), 1,114 individuals missing depression screener variables were excluded. Also excluded were 388 pregnant women or women with a positive pregnancy urine test, 106 individuals missing BMI, and 5 participants whose response to the education level question was “don’t know” or “refused.” The final study sample consisted of 9,714 individuals (82.4% of adult NHANES participants in 2005-2008).

### Statistical Analysis

All analyses were conducted using SAS 9.2 (SAS Institute, Inc., Cary, NC) with SUDAAN 10.0.0 (RTI International, Research Triangle Park, NC), which accounted for the complex sampling design and applied the MEC sample weights for all analyses. The proportion of participants with depression (PHQ-9 score  $\geq 10$  or PHQ-2 score  $\geq 3$ ) and the odds ratio (OR) and 95% confidence intervals (CI) for the likelihood of depression associated with SDB symptoms were obtained from sex-specific multivariate logistic regression analyses that adjusted for race/ethnicity, age category, education level, and BMI category. We performed similar analyses to assess the association between a physician diagnosis of sleep apnea and the frequency of SDB symptoms. We present results of analyses in which responses of “don’t know” for SDB questions were coded as “missing.” Coding “don’t know” responses as “never” gave similar results.

### RESULTS

Weighted population characteristics are shown in Table 2. Approximately 72% of participants were non-Hispanic white, 16% were aged  $\geq 65$  years, and 25% were college graduates. Overall, 72% of men and 63% of women were overweight or obese. In this study, 6.0% of men and 3.1% of women reported a diagnosis of sleep apnea by a health professional and 37.2% of men reported snoring  $\geq 5$  nights/week, compared to 22.4% of women. Most participants reported that they never snort/stop breathing, but 22.7% of men and 15.4% of women reported snorting/stopping breathing at least one night/week, while 7.1% of men and 4.3% of women reported snorting/stopping breathing  $\geq 5$  nights/week. More women (8.4%) than men (5.0%) were depressed (PHQ-9 score  $\geq 10$ ).

Among men, the prevalence of physician-diagnosed sleep apnea was lower in those who reported snoring 1-2 nights/week or 3-4 nights/week compared to never snoring (Table 3). Among women, physician-diagnosed sleep apnea prevalence was higher in those who reported snoring  $\geq 5$  nights/week compared to never-snorers. Among both men and women, the prevalence of physician-diagnosed sleep apnea increased with higher frequency of snorting/stopping breathing (linear trend  $P$ -value  $< 0.0001$ ). More than 80% of participants who reported snorting/stopping breathing  $\geq 5$  nights/week had *not* been diagnosed with sleep apnea.

Among men, the prevalence of depression (PHQ-9 score  $\geq 10$ ) was 2 times higher ( $P < 0.05$ ) among those who reported physician-diagnosed sleep apnea (adjusted odds ratio [OR] = 2.4 [95% CI: 1.5, 3.6]) (Table 4). Although snoring was not associated with depression among men, frequency of snorting/stopping

**Table 2**—Selected population characteristics: NHANES, 2005-2008

Characteristic	Men		Women	
	n <sup>a</sup>	% <sup>b</sup>	n <sup>a</sup>	% <sup>b</sup>
Total	4,947		4,767	
Race/Ethnicity				
White, non-Hispanic	2,418	71.5	2,215	71.8
Black, non-Hispanic	1,091	10.5	1,084	11.8
Mexican-American	931	9.1	894	7.0
Other/Multiracial	507	8.9	574	9.4
Age				
18-24	778	13.7	700	11.4
25-34	745	17.9	668	15.7
35-44	794	19.5	771	19.5
45-54	791	21.7	792	21.0
55-64	705	13.1	747	14.4
65+	1,134	14.2	1,089	18.1
Education Level				
< High school diploma	1,523	20.0	1,330	17.6
High school diploma	1,257	26.1	1,192	25.1
Some college	1,258	28.8	1,387	32.1
College graduate	909	25.1	858	25.2
BMI <sup>c</sup>				
Underweight	69	1.2	113	2.4
Normal weight	1,391	27.3	1,466	35.2
Overweight	1,916	39.3	1,356	27.5
Obese-Class I	1,004	21.0	926	17.3
Obese-Class II	353	7.1	530	10.3
Obese-Class III	214	4.2	376	7.4
Sleep Apnea Diagnosis				
Yes	269	6.0	140	3.1
No	4,678	94.0	4,627	96.9
Snore				
Don't know <sup>d</sup>	415	7.1	642	11.3
Never	1,179	21.9	1,469	31.6
1-2 nights/week	783	16.4	817	18.7
3-4 nights/week	848	17.3	750	16.0
$\geq 5$ nights/week	1,722	37.2	1,089	22.4
Snort/Stop Breathing				
Don't know <sup>d</sup>	371	7.2	434	7.5
Never	3,495	70.1	3,608	77.2
1-2 nights/week	423	8.6	325	7.1
3-4 nights/week	341	7.0	215	4.0
$\geq 5$ nights/week	317	7.1	185	4.3
Depression				
Using PHQ-9 criteria <sup>e</sup>				
No	4,648	95.0	4,286	91.6
Yes	299	5.0	481	8.4
Using PHQ-2 criteria <sup>f</sup>				
No	4,595	94.1	4,294	92.1
Yes	352	5.9	473	7.9

<sup>a</sup>Unweighted n's. <sup>b</sup>Weighted percentage. <sup>c</sup>Underweight (BMI  $< 18.5$ ), Normal weight ( $18.5 \leq \text{BMI} < 25$ ), Overweight ( $25 \leq \text{BMI} < 30$ ), Obese-Class I ( $30 \leq \text{BMI} < 35$ ), Obese-Class II ( $35 \leq \text{BMI} < 40$ ), Obese-Class III (BMI  $\geq 40$ ). Due to the small number of underweight individuals, the underweight and normal weight BMI categories were pooled in logistic regression analysis. <sup>d</sup>Responses of “don’t know” for either symptom of sleep-disordered breathing were coded as “missing.” <sup>e</sup>Total score  $\geq 10$  on full 9-item screener (PHQ-9). <sup>f</sup>Total score  $\geq 3$  on 2-item screener (PHQ-2).

**Table 3**—Prevalence (%) of physician-diagnosed sleep apnea<sup>a</sup> by frequency of selected sleep disordered breathing symptoms: NHANES, 2005–2008

	Men			Women		
	% (Unadjusted) <sup>b</sup>	% <sup>c</sup>	OR <sup>c</sup> (95% CI)	% (Unadjusted) <sup>b</sup>	% <sup>c</sup>	OR <sup>c</sup> (95% CI)
Snore						
Never	6.8	9.2	Referent	1.5	2.5	Referent
1-2 nights/wk	4.2	5.0	0.5 (0.3-0.9)	1.2	1.6	0.6 (0.2-1.6)
3-4 nights/wk	4.1	4.2	0.4 (0.2-0.7)	3.0	2.6	1.0 (0.5-2.1)
≥ 5 nights/wk	8.0	6.5	0.7 (0.4-1.1)	7.7	4.7	2.0 (1.1-3.6)
Snort/stop breathing						
Never	3.3	3.7	Referent	1.2	1.3	Referent
1-2 nights/wk	9.2	8.2	2.5 (1.6-3.8)	4.5	4.0	3.3 (1.5-7.2)
3-4 nights/wk	12.1	9.7	3.1 (1.7-5.7)	11.4	9.0	8.6 (4.0-18.3)
≥ 5 nights/wk	25.9	18.2	7.1 (4.4-11.6)	27.6	15.9	8.5 (9.6-35.5)

<sup>a</sup>Self-report of physician-diagnosed sleep apnea. <sup>b</sup>Weighted, unadjusted percentage. <sup>c</sup>Percentages and odds ratios (OR) are weighted and adjusted for age, race/ethnicity, education, and body mass index.

**Table 4**—Prevalence (%) of depression among adults aged ≥ 18 years by sleep apnea diagnosis and selected sleep disordered breathing symptoms: NHANES, 2005–2008

Depression (PHQ-9 criteria <sup>a</sup> )	Men			Women		
	% <sup>b</sup>	OR <sup>b</sup> (95% CI)	Linear trend P-value <sup>c</sup>	%	OR (95% CI)	Linear trend P-value
Sleep apnea diagnosis?						
Yes	10.2	2.4 (1.5-3.6)		28.3	5.2 (2.7-9.9)	
No	4.7	Referent		7.8	Referent	
Snore						
Never	4.9	Referent		7.8	Referent	
1-2 nights/wk	3.4	0.7 (0.4-1.3)		7.4	1.0 (0.6-1.4)	
3-4 nights/wk	4.9	1.0 (0.6-1.7)		7.1	0.9 (0.6-1.3)	
≥ 5 nights/wk	5.3	1.1 (0.7-1.7)	0.384	10.9	1.5 (1.0-2.2)	0.115
Snort/stop breathing						
Never	3.7	Referent		7.3	Referent	
1-2 nights/wk	6.3	1.8 (1.2-2.7)		8.9	1.3 (0.8-2.0)	
3-4 nights/wk	8.7	2.6 (1.5-4.5)		18.5	3.1 (1.8-5.0)	
≥ 5 nights/wk	10.2	3.1 (1.8-5.2)	< 0.001	18.1	3.0 (1.6-5.4)	< 0.001
Depression (PHQ-2 criteria <sup>d</sup> )	Men			Women		
	%	OR (95% CI)	Linear trend P-value	%	OR (95% CI)	Linear trend P-value
Sleep apnea diagnosis?						
Yes	8.5	1.5 (0.9-2.5)		24.7	4.5 (2.6-7.8)	
No	5.8	Referent		7.4	Referent	
Snore						
Never	6.9	Referent		6.9	Referent	
1-2 nights/wk	4.5	0.6 (0.4-1.0)		6.4	0.9 (0.6-1.5)	
3-4 nights/wk	5.6	0.8 (0.5-1.3)		7.1	1.0 (0.6-1.7)	
≥ 5 nights/wk	6.0	0.9 (0.6-1.2)	0.660	10.7	1.7 (1.1-2.4)	0.019
Snort/stop breathing						
Never	5.0	Referent		6.9	Referent	
1-2 nights/wk	6.4	1.3 (0.8-2.2)		9.4	1.4 (0.9-2.2)	
3-4 nights/wk	9.6	2.1 (1.3-3.3)		15.1	2.5 (1.5-4.0)	
≥ 5 nights/wk	10.1	2.2 (1.2-3.8)	0.008	17.2	2.9 (1.7-5.0)	< 0.001

<sup>a</sup>Depression based on total score ≥ 10 on full 9-item screener (PHQ-9). <sup>b</sup>Percentages and odds ratios (OR) are weighted and adjusted for age, race/ethnicity, education, and body mass index. <sup>c</sup>P-value for Wald F test for linear trend by frequency of SDB symptoms. <sup>d</sup>Depression based on total score ≥ 3 on 2-item screener (PHQ-2).

breathing was positively associated with a higher likelihood of depression (linear trend P-value < 0.001), with an adjusted OR of 3.1 (95% CI: 1.8, 5.2) for ≥ 5 nights/week compared to never

snort/stop breathing. Among women, the prevalence of depression was 5 times higher (P < 0.05) among those who reported physician-diagnosed sleep apnea (OR = 5.2 [95% CI: 2.7, 9.9]).



**Table 5**—Prevalence (%) of depression among adults aged  $\geq 18$  years without physician-diagnosed sleep apnea by selected sleep-disordered breathing symptoms: NHANES, 2005–2008

Depression (PHQ-9 criteria <sup>a</sup> )	Men			Women		
	% <sup>b</sup>	OR <sup>b</sup> (95% CI)	Linear trend P-value <sup>c</sup>	%	OR (95% CI)	Linear trend P-value
Snore						
Never	4.1	Referent		7.5	Referent	
1-2 nights/wk	3.4	0.8 (0.4-1.6)		7.4	1.0 (0.7-1.5)	
3-4 nights/wk	4.5	1.1 (0.7-1.9)		5.9	0.8 (0.5-1.1)	
$\geq 5$ nights/wk	5.2	1.3 (0.8-2.0)	0.124	9.5	1.3 (0.9-1.9)	0.392
Snort/stop breathing						
Never	3.5	Referent		7.0	Referent	
1-2 nights/wk	5.4	1.6 (0.9-2.9)		8.8	1.3 (0.8-2.1)	
3-4 nights/wk	8.0	2.4 (1.5-4.0)		15.9	2.6 (1.5-4.7)	
$\geq 5$ nights/wk	11.5	3.7 (2.2-6.4)	< 0.001	14.0	2.3 (1.2-4.3)	0.009
Depression (PHQ-2 criteria <sup>d</sup> )	Men			Women		
	%	OR (95% CI)	Linear trend P-value	%	OR (95% CI)	Linear trend P-value
Snore						
Never	6.5	Referent		6.6	Referent	
1-2 nights/wk	4.6	0.7 (0.4-1.1)		6.2	0.9 (0.6-1.5)	
3-4 nights/wk	5.5	0.8 (0.5-1.4)		6.1	0.9 (0.6-1.5)	
$\geq 5$ nights/wk	5.9	0.9 (0.6-1.2)	0.795	9.8	1.6 (1.1-2.2)	0.032
Snort/stop breathing						
Never	5.0	Referent		6.6	Referent	
1-2 nights/wk	5.4	1.1 (0.6-1.9)		9.1	1.4 (0.9-2.2)	
3-4 nights/wk	9.7	2.1 (1.3-3.5)		13.8	2.3 (1.4-3.9)	
$\geq 5$ nights/wk	11.3	2.5 (1.5-4.3)	0.002	13.7	2.3 (1.3-4.2)	0.003

<sup>a</sup>Depression based on total score  $\geq 10$  on full 9-item screener (PHQ-9). <sup>b</sup>Percentages and odds ratios (OR) are weighted and adjusted for age, race/ethnicity, education, and body mass index. <sup>c</sup>P-value for Wald F test for linear trend by frequency of SDB symptoms. <sup>d</sup>Depression based on total score  $\geq 3$  on 2-item screener (PHQ-2).

As among men, snoring was not associated with depression among women, but the frequency of snorting/stopping breathing was positively associated with a higher likelihood of depression (linear trend P-value < 0.001), with an adjusted OR of 3.0 (95% CI: 1.6, 5.4) for  $\geq 5$  nights/week compared to never snort/stop breathing. Using the PHQ-2 criteria for depression, the effects of sleep apnea diagnosis on depression were somewhat attenuated for both men and women, such that the effect was no longer significant for men. The effect of snorting/stopping breathing was slightly attenuated for men but largely unchanged for women. When limiting our analyses to participants without physician-diagnosed sleep apnea, the frequency of snorting/stopping breathing remained positively associated with a higher likelihood of depression for both men and women (Table 5).

The likelihood of a positive response to nearly all individual PHQ-9 items was significantly higher ( $P < 0.05$ ) if individuals reported snorting/stopping breathing  $\geq 1$  night/week for both men and women (Table 6). Snorting/stopping breathing was most strongly associated with positive responses for “hopeless” (OR = 1.9 [95% CI: 1.4, 2.6] for men and OR = 2.5 [95% CI: 1.8, 3.4] for women). As expected, the prevalence of reporting “sleep difficulties” and “low energy” was higher for those reporting snorting/stopping breathing  $\geq 1$  night/week.

## DISCUSSION

In this large, nationally representative study population, we found that the likelihood of depression was significantly higher

for men and women who reported a previous diagnosis of sleep apnea, which is in agreement with prior research.<sup>12,21</sup> In addition, men and women who reported that they snort, gasp, or stop breathing while they sleep were also more likely to be depressed. The likelihood of depression also increased with the frequency of snorting/stopping breathing.

There is evidence from intervention studies to suggest a causal link between OSA and depression. In their longitudinal analysis of data from the Wisconsin Sleep Cohort Study, Peppard et al. found a dose-response relationship between SDB severity and odds of subsequently developing depression.<sup>16</sup> Numerous studies have documented improvements in depression after treatment of OSA with continuous positive airway pressure (CPAP), the most common treatment for OSA.<sup>22-30</sup> These studies have demonstrated positive results after short-term treatment (two weeks to three months)<sup>22,24-26,29</sup> or longer-term treatment (six months to a year).<sup>27,28,30</sup> Studies have also observed a positive effect on mood or depression with alternative treatments of SDB, including use of oral appliances and surgery, although these studies have been small and/or have failed to include appropriate control groups.<sup>31-33</sup> Borak et al.<sup>34</sup> found no statistically significant improvement in depression as assessed using the Beck Depression Index score after three and twelve months of CPAP treatment, but the study was small (20 patients), and the mean baseline BDI score was within the “not depressed” range.

Suggested pathways linking OSA to an increased risk for depression include sleep fragmentation and hypoxia. Episodic

**Table 6**—Comparison of the prevalence of positive responses<sup>a</sup> to individual items on depression screener between adults who reported never snorting/stopping breathing and those who reported snorting/stopping breathing  $\geq 1$  night/week: NHANES, 2005-2008

Men		Never	$\geq 1$ night/week	
PHQ-9 Item	%	%	OR <sup>b</sup> (95% CI)	
Disinterested	4.2	6.9	1.7 (1.2-2.4)	
Hopeless	3.7	6.6	1.9 (1.4-2.6)	
Sleep difficulties	10.2	15.4	1.6 (1.3-2.0)	
Low energy	9.5	16.1	1.9 (1.4-2.4)	
Appetite issues	4.4	7.5	1.8 (1.1-2.9)	
Feel like failure	2.6	4.6	1.8 (1.2-2.6)	
Difficulty concentrating	3.2	5.3	1.7 (1.1-2.6)	
Slow or fidgety	2.1	3.0	1.5 (0.9-2.4)	
Better off dead	2.7	4.0	1.5 (1.0-2.3)	
Women		Never	$\geq 1$ night/week	
PHQ-9 Item	%	%	OR <sup>b</sup> (95% CI)	
Disinterested	5.3	9.7	2.0 (1.2-3.2)	
Hopeless	5.7	12.8	2.5 (1.8-3.4)	
Sleep difficulties	15.0	19.6	1.4 (1.0-1.9)	
Low energy	15.8	25.2	1.8 (1.4-2.4)	
Appetite issues	8.4	13.4	1.7 (1.2-2.4)	
Feel like failure	4.5	10.0	2.4 (1.8-3.3)	
Difficulty concentrating	4.9	8.7	1.9 (1.4-2.6)	
Slow or fidgety	2.7	5.3	2.1 (1.2-3.6)	
Better off dead	2.7	5.1	1.9 (1.2-3.2)	

<sup>a</sup>For the first eight items, a positive response is at least "more than half the days." For the last item, a positive response is any response other than "not at all." The weighted percentage is adjusted for age, race/ethnicity, education, and body mass index. <sup>b</sup>Odds ratio (OR) with never snort/stop breathing as the referent group, adjusted for age, race/ethnicity, education, and body mass index in a multivariate logistic regression model.

hypoxia from OSA has been linked to altered neuronal activity and decreased gray and white matter in the brain, possibly through induction of oxidative stress, inflammation, or endoplasmic reticulum stress.<sup>35</sup> Support for these mechanisms has come from correlational studies as well as intervention studies, although results have not been consistent. Some of these studies found that higher depression scores were associated with measures of sleep fragmentation,<sup>11,17</sup> while another small study showed improved overall psychological well-being for either CPAP or oxygen supplementation, but improved depression scores only with oxygen supplementation.<sup>29</sup> Of note, experimentally induced sleep fragmentation changed mood in one study.<sup>36</sup>

Given the high prevalence and underdiagnosis of both SDB and depression, screening for each of these disorders in the presence of the other has the potential to alleviate some of the burden of undiagnosed and untreated disease. As discussed above, treatment of underlying SDB in depressed individuals may improve depression outcomes, especially if sleepiness is a chief complaint. Habukawa and colleagues<sup>25</sup> focused their study on patients with residual depression after pharmacotherapy and found that two months of CPAP improved their depression scores. This finding warrants further investigation. A possible added benefit to screening patients with SDB for depression is that treatment for depression may improve CPAP

adherence. Depression has been found to be associated with low patient adherence to treatment for diabetes,<sup>37</sup> asthma,<sup>38</sup> and chronic obstructive pulmonary disease.<sup>39</sup> Baseline depression has been found to be a predictor of CPAP compliance in one study,<sup>40</sup> but not in others.<sup>41-43</sup>

The cross-sectional nature of the study did not permit us to assess causality in the relationship between SDB and depression. Another limitation of the study was that we had to rely on self-report of symptoms and bed partners were not asked about participants' symptoms. Since SDB symptoms occur during sleep, some individuals may not be aware of the symptoms or may underestimate symptom frequency, especially if they sleep alone. In addition, for individuals reporting an OSA diagnosis, there is no information about treatment for OSA. For this reason, we repeated our analyses to include only participants without a diagnosis of sleep apnea, who we reasonably assume are not being treated for OSA. There is also no information about treatment for depression.

In contrast to previous research that has investigated patient populations, we analyzed the association between SDB-specific symptoms and depression in a large, population-based sample rather than in a patient sample. This is an important feature of our study since both SDB and depression are considerably underdiagnosed. We also evaluated frequency of SDB symptoms in addition to OSA diagnosis and were able to control for BMI. There are many tools that have been used to determine depression. Some, such as the Symptom Checklist-90 and the Minnesota Multiphasic Personality Inventory, are better measures of stable personality traits and are not specific to depression, whereas the PHQ-9, used in our study, is specific to depression and is more sensitive to changes in symptoms.<sup>10</sup>

## CONCLUSION

Frequent snorting/stopping breathing, but not snoring, was associated with higher prevalence of probable major depression, even after adjustment for BMI. Additional intervention research is needed to determine whether routine screening for and referral for treatment of depression by sleep specialists may be indicated. Further intervention studies are necessary to determine if treatment of depression may result in less fatigue and higher quality of life for patients than treatment for sleep apnea alone. Studies to determine if treatment of depression may improve CPAP compliance may also be called for. Mental health professionals may consider asking patients about SDB symptoms since diagnosis and treatment of SDB by a sleep specialist may improve depressive symptoms. Mental health professionals often ask about certain sleep problems, such as unrefreshing sleep and insomnia, but likely do not realize that SDB may have an impact on their patients' mental health. Additional intervention research is needed to determine whether treatment of SDB among depressed patients will reduce the need for antidepressant medication and improve outcomes. Sleep is essential and healthy sleep should be as important as healthy nutrition, physical activity, and smoking cessation in promoting overall health.

## ACKNOWLEDGMENTS

Dr. Wheaton was supported through a cooperative agreement between the Association for Prevention Teaching and Research

(APTR) and the Centers for Disease Control and Prevention (CDC), award number 3U50CD300860.

## DISCLOSURE STATEMENT

This was not an industry supported study. The authors have indicated no financial conflicts of interest. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

## REFERENCES

1. Al Lawati NM, Patel SR, Ayas NT. Epidemiology, risk factors, and consequences of obstructive sleep apnea and short sleep duration. *Prog Cardiovasc Dis* 2009;51:285-93.
2. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230-5.
3. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 2002;165:1217-39.
4. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med* 2000;342:1378-84.
5. Capampangan DJ, Wellik KE, Parish JM, et al. Is obstructive sleep apnea an independent risk factor for stroke? A critically appraised topic. *Neurologist* 2010;16:269-73.
6. Arzt M, Young T, Finn L, Skatrud JB, Bradley TD. Association of sleep-disordered breathing and the occurrence of stroke. *Am J Respir Crit Care Med* 2005;172:1447-51.
7. Selim B, Won C, Yaggi HK. Cardiovascular consequences of sleep apnea. *Clin Chest Med* 2010;31:203-20.
8. Aloia MS, Arnedt JT, Davis JD, Riggs RL, Byrd D. Neuropsychological sequelae of obstructive sleep apnea-hypopnea syndrome: a critical review. *J Int Neuropsychol Soc* 2004;10:772-85.
9. Yamamoto H, Akashiba T, Kosaka N, Ito D, Horie T. Long-term effects nasal continuous positive airway pressure on daytime sleepiness, mood and traffic accidents in patients with obstructive sleep apnoea. *Respir Med* 2000;94:87-90.
10. Saunamaki T, Jehkonen M. Depression and anxiety in obstructive sleep apnea syndrome: a review. *Acta Neurol Scand* 2007;116:277-88.
11. Yue W, Hao W, Liu P, Liu T, Ni M, Guo Q. A case-control study on psychological symptoms in sleep apnea-hypopnea syndrome. *Can J Psychiatry* 2003;48:318-23.
12. Kales A, Caldwell AB, Cadieux RJ, Vela-Bueno A, Ruch LG, Mayes SD. Severe obstructive sleep apnea--II: Associated psychopathology and psychosocial consequences. *J Chronic Dis* 1985;38:427-34.
13. Ohayon MM. The effects of breathing-related sleep disorders on mood disturbances in the general population. *J Clin Psychiatry* 2003;64:1195-200.
14. Sharafkhaneh A, Giray N, Richardson P, Young T, Hirshkowitz M. Association of psychiatric disorders and sleep apnea in a large cohort. *Sleep* 2005;28:1405-11.
15. Sivertsen B, Overland S, Glozier N, Bjorvatn B, Maeland JG, Mykletun A. The effect of OSAS on sick leave and work disability. *Eur Respir J* 2008;32:1497-503.
16. Peppard PE, Szklo-Coxe M, Hla KM, Young T. Longitudinal association of sleep-related breathing disorder and depression. *Arch Intern Med* 2006;166:1709-15.
17. Deldin PJ, Phillips LK, Thomas RJ. A preliminary study of sleep-disordered breathing in major depressive disorder. *Sleep Med* 2006;7:131-9.
18. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606-13.
19. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care* 2003;41:1284-92.
20. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults--the evidence report. *Obes Res* 1998;6 Suppl 2:S1S-209S.
21. McCall WV, Harding D, O'Donovan C. Correlates of depressive symptoms in patients with obstructive sleep apnea. *J Clin Sleep Med* 2006;2:424-6.
22. Means MK, Lichstein KL, Edinger JD, et al. Changes in depressive symptoms after continuous positive airway pressure treatment for obstructive sleep apnea. *Sleep Breath* 2003;7:31-42.
23. Millman RP, Fogel BS, McNamara ME, Carlisle CC. Depression as a manifestation of obstructive sleep apnea: reversal with nasal continuous positive airway pressure. *J Clin Psychiatry* 1989;50:348-51.
24. Kawahara S, Akashiba T, Akahoshi T, Horie T. Nasal CPAP improves the quality of life and lessens the depressive symptoms in patients with obstructive sleep apnea syndrome. *Intern Med* 2005;44:422-7.
25. Habukawa M, Uchimura N, Kakuma T, et al. Effect of CPAP treatment on residual depressive symptoms in patients with major depression and coexisting sleep apnea: Contribution of daytime sleepiness to residual depressive symptoms. *Sleep Med* 2010;11:552-7.
26. Sanchez AI, Buena-Casal G, Bermudez MP, Casas-Maldonado F. The effects of continuous positive air pressure treatment on anxiety and depression levels in apnea patients. *Psychiatry Clin Neurosci* 2001;55:641-6.
27. Ramos Platon MJ, Espinar Sierra J. Changes in psychopathological symptoms in sleep apnea patients after treatment with nasal continuous positive airway pressure. *Int J Neurosci* 1992;62:173-95.
28. Joseph S, Zuriqat M, Husari A. Sustained improvement in cognitive and emotional status of apneic patients after prolonged treatment with positive airway pressure. *South Med J* 2009;102:589-94.
29. Bardwell WA, Norman D, Ancoli-Israel S, et al. Effects of 2-week nocturnal oxygen supplementation and continuous positive airway pressure treatment on psychological symptoms in patients with obstructive sleep apnea: a randomized placebo-controlled study. *Behav Sleep Med* 2007;5:21-38.
30. Schwartz DJ, Karatinos G. For individuals with obstructive sleep apnea, institution of CPAP therapy is associated with an amelioration of symptoms of depression which is sustained long term. *J Clin Sleep Med* 2007;3:631-5.
31. Saletu A, Anderer P, Parapatics S, Matthai C, Matejka M, Saletu B. Effects of a mandibular repositioning appliance on sleep structure, morning behavior and clinical symptomatology in patients with snoring and sleep-disordered breathing. *Neuropsychobiology* 2007;55:184-93.
32. Mosko S, Zetin M, Glen S, et al. Self-reported depressive symptomatology, mood ratings, and treatment outcome in sleep disorders patients. *J Clin Psychol* 1989;45:51-60.
33. Klonoff H, Fleetham J, Taylor DR, Clark C. Treatment outcome of obstructive sleep apnea. Physiological and neuropsychological concomitants. *J Nerv Ment Dis* 1987;175:208-12.
34. Borak J, Cieslicki JK, Koziej M, Matuszewski A, Zielinski J. Effects of CPAP treatment on psychological status in patients with severe obstructive sleep apnoea. *J Sleep Res* 1996;5:123-7.
35. Lim DC, Veasey SC. Neural injury in sleep apnea. *Curr Neurol Neurosci Rep* 2010;10:47-52.
36. Martin SE, Wraith PK, Deary IJ, Douglas NJ. The effect of nonvisible sleep fragmentation on daytime function. *Am J Respir Crit Care Med* 1997;155:1596-601.
37. Katon W, Russo J, Lin EH, et al. Diabetes and poor disease control: is comorbid depression associated with poor medication adherence or lack of treatment intensification? *Psychosom Med* 2009;71:965-72.
38. Bosley CM, Fosbury JA, Cochrane GM. The psychological factors associated with poor compliance with treatment in asthma. *Eur Respir J* 1995;8:899-904.
39. Wilson I. Depression in the patient with COPD. *Int J Chron Obstruct Pulmon Dis* 2006;1:61-4.
40. Edinger JD, Carwile S, Miller P, Hope V, Mayti C. Psychological status, syndromatic measures, and compliance with nasal CPAP therapy for sleep apnea. *Percept Mot Skills* 1994;78:1116-8.
41. Lewis KE, Seale L, Bartle IE, Watkins AJ, Ebden P. Early predictors of CPAP use for the treatment of obstructive sleep apnea. *Sleep* 2004;27:134-8.
42. Poulet C, Veale D, Arnol N, Levy P, Pepin JL, Tyrrell J. Psychological variables as predictors of adherence to treatment by continuous positive airway pressure. *Sleep Med* 2009;10:993-9.
43. Stepnowsky CJ Jr., Bardwell WA, Moore PJ, Ancoli-Israel S, Dimsdale JE. Psychologic correlates of compliance with continuous positive airway pressure. *Sleep* 2002;25:758-62.