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Association Between Insomnia Symptoms and Moderately Severe to Severe Depression in the US Adult Population

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Degree to be Awarded: MPH
Executive MPH

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Abstract

Association Between Insomnia Symptoms and Moderately Severe to Severe Depression in the US Adult Population

By Keith A. Szymanski

Study Objective: To evaluate whether each of the following International Classification of Sleep Disorders (ICSD) insomnia symptoms: difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS), or nonrestorative sleep (NRS) are predictive of moderately severe to severe depression [as determined by a PHQ-9 (Physician Health Questionnaire-9) score of $\geq$15].

Methods: Retrospective cross-sectional study was conducted which included survey respondents representative of the US adult population. Respondents with a PHQ-9 score were stratified into two groups: PHQ-9 score $\leq$ 4 (no or minimal depression) [NMD], PHQ-9 score $\geq$ 15 (moderately severe to severe depression) [MSS]. Multivariate logistic regression was utilized to determine which specific insomnia symptoms were predictive of depression severity.

Results: 2,431 adults completed the survey. The overall response rate was 80.4%. 51.6% of respondents were in the NMD group and 16.2% of respondents were in the MSS group. Individuals in the MSS group reported more insomnia symptoms (DIS, DMS, NRS), when compared to the NMD group (47.32% vs. 4.90%, $p < 0.05$), 53.93% vs. 9.53%, $p < 0.05$, 77.16% vs. 47.08%, $p < 0.05$, respectively). DIS, DMS, and NRS were significantly associated with MSS (OR=5.20, 95% CI: 3.10-8.74, $p < 0.05$, OR=4.16, 95% CI: 2.66-6.52, $p < 0.05$, OR=1.89, 95% CI :1.37-2.61, respectively).

Conclusions: All three insomnia symptoms were associated with depression severity. Of particular interest is the high percent of individuals reporting nonrestorative sleep which can occur in the absence of other insomnia symptoms. Increasing the awareness of all pertinent insomnia symptoms may aid clinicians in tailoring treatments plans to the specific needs of each patient.

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Introduction:

Approximately 80% of patients with depression experience insomnia symptoms.[1] A complex bidirectional relationship between insomnia and depression has been demonstrated by numerous studies.[2] In particular, insomnia has been associated with the duration of depression, developing a subsequent depressive episode, and relapse. Siverstein et al conducted a prospective population study whereby 24,715 individuals were surveyed to determine the directional association between insomnia and depression.[3] The investigators concluded that the disorders predicted the onset of each other. This bidirectional relationship continues to pose a challenge to treating clinicians with relatively 30% of patients with a history of depression reporting unresolved levels of fatigue and incurring significantly greater healthcare costs.[4]

Despite the many epidemiological studies investigating the association between insomnia and depression, few studies have addressed the association between specific insomnia symptoms and depression severity. Taylor et al conducted a cross-sectional retrospective study involving 752 adult community individuals who completed questionnaires on general health, sleep, depression, and anxiety.[5] Sleep diaries were used for reporting insomnia symptoms and the Beck Depression Inventory was utilized to assess depression. Insomnia was defined as people self-reporting insomnia for at least 6 months, a daytime complaint, and occurring at least 3 nights/week either sleep onset latency ($\geq$31 minutes) [SOL], wake time after sleep onset ($\geq$31 minutes) [WASO], or a combination of the two symptoms. The investigators reported that an increase in insomnia frequency and the mean number of night awakenings were associated with

increased depression severity scores. Also, individuals with combined SOL and WASO had greater depression severity compared to SOL and WASO individually.

Froese et al completed a cross-sectional survey study in an adult, indigenous, North American population which was designed to evaluate the relationship between sleep symptoms and depression.[6] The sleep habits and symptoms of 432 individuals were assessed by a questionnaire and the Epworth Sleepiness Scale. Individuals were categorized as having insomnia symptoms if they responded "every night or almost every night" to the following item on the questionnaire: How often do you have difficulty falling asleep, have frequent awakenings during the night, wake too early and are unable to get back to sleep, or wake feeling unrefreshed? The Physician Health Questionnaire (PHQ-9) was utilized for determining depression severity. The mean PHQ-9 score was 4.86 and 7.20% of respondents had a PHQ-9 score $\geq$15. Insomnia symptoms were associated with an increasing PHQ-9 score. However, individual insomnia symptoms were not reported in this study.

The objective of this current study is to evaluate whether each of the following International Classification of Sleep Disorders (ICSD) insomnia symptoms: difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS), or non-restorative sleep (NRS)] are predictive of moderately severe to severe depression (as determined by a PHQ-9 score of $\geq$15).[7]

Methods:

A retrospective cross-sectional study was conducted which included survey respondents representative of the US adult population. All study methods were reviewed and approved by the Emory University Institutional Review Board.

Participants

Acumen Health Research Institute (AHRI) is a 501(c)(3) non-profit organized in 2016 to assess healthcare, health-related quality of life and resource utilization in the United States. The goal of AHRI is to help decision makers understand the burden of disease and identify gaps for improvement. AHRI's 2016 National Health Research Study (NHRS) surveyed respondents recruited from 10 validated internet panels utilizing a random stratified sampling framework to ensure demographic composition similar to the US adult population. AHRI collected the data as a study assessing the feasibility of collecting a nationally representative sample to assess general health of the US adult population. The internet surveys included the following pertinent data fields: demographics, diagnoses (comorbidities), medication use, and healthcare resource utilization. Responses were weighted by region, gender, and age to be representative of the US Census. Taylor Series Linearization method for estimating population characteristics from complex sample survey data was utilized for the weighting tests. An analysis was completed comparing the NHRS survey results to the US 2010 census. Similar results were reported for both surveys. Weighted results were reported so that comparisons could be made to additional depression and/or insomnia cohort studies that were representative of the US population.

Variables and Measurement

The primary independent variables were specific insomnia symptoms. The following insomnia symptoms were included within the NHRS survey: How many nights per week do you have difficulty falling asleep? How many nights per week do you have trouble staying asleep? How many nights per week have you had restorative sleep? To align

with ICSD criteria for chronic insomnia disorder the duration of symptoms was defined as greater than or equal to 3 days per week.

Depression severity was the primary dependent variable. Depression severity was assessed utilizing the PHQ-9.[8] The PHQ-9 total score range is 0 to 27. Scores ≤4 represent minimal depression whereas scores ≥15 represent moderately severe to severe depression.

A PubMed literature search and expert clinical opinion were used to identify additional variables associated insomnia and/or depression.[9,10] NHRS survey comorbidities included: alcohol or drug problem, fibromyalgia, gout, hypertension, hyperlipidemia, asthma, chronic obstructive pulmonary disease, type 2 diabetes, cancer, migraine, obesity, overactive bladder, osteoarthritis, hypothyroidism, cancer, sleep apnea, anxiety [as measured by the General Anxiety Disorder-7 (GAD-7) questionnaire], multiple sclerosis, and kidney disease. The following respondent demographics were reported: mean age, gender (male/female), race and ethnicity (White, Black, Other, Hispanic origin), marital status (married and female, married and male), health insurance status (insured/not insured), education level, employment status.

Analysis

Respondents with a PHQ-9 score were stratified into two groups: PHQ-9 score ≤ 4 (minimal depression), PHQ-9 score ≥ 15 (moderately severe to severe depression). Chi-squares for categorical data and general linear models were utilized to analyze insomnia symptoms, respondent demographics, and comorbidities.

Multivariate logistic regression modeling was utilized to predict the factors associated with a PHQ-9 score ≥15. To address confounding, the logistic model controlled for all

of the variables in the univariate analyses which included: demographics (sex, race, age, education level, employment status, insurance coverage, geographic region), and clinical characteristics (insomnia symptoms and comorbidities). Odds ratios, 95% CIs, and p-values were reported for all model variables.

Results:

2,413 adults (age ≥ 18 years) completed the survey. The overall response rate was 80.4%. Approximately 50% of respondents had no or minimal depression (NMD) whereas 16.2% reported moderately severe to severe depression (MSS). The remaining 32.2% of respondents had mild or moderate depression (Table 1).

Table 1: Unweighted and Weighted PHQ-9 Depression Classifications

		Unweighted		Weighted	
Depression Classification	**PHQ-9 Score**	**n**	**Percent, %**	**N**	**Percent, %**
No or minimal depression	0 - 4	1219	50.5	121,093,270	51.6
Mild or moderate depression	5 - 14	802	33.2	75,495,901	32.2
Moderately severe to severe depression	≥ 15	392	16.2	37,974,900	16.2
Total		2413	100.0	234,564,071	100.0

Descriptive respondent characteristics stratified by depression severity (NMS vs. MSS) are included in Table 2. The MSS group had a higher percent of individuals from Hispanic origin compared to the NMS group (16.21% vs. 7.94%, $p < 0.05$). The MSS group was significantly younger than the NMS group (mean age [SD] = 39.80[14.12] vs. 50.17[16.90], $p < 0.05$). A lower number of respondents were married and male when comparing the MSS and NMS groups (20.09% vs. 29.26%, $p < 0.05$).

Differences between the MSS and NMS groups were also reported for respondents with no educational degree (56.69% vs. 42.66%, $p < 0.05$), employed full-time (33.39% vs. 38.03%, $p < 0.05$), and those individuals with insurance coverage (81.77% vs. 89.72, $p < 0.05$).

The two groups were comparable with regards to sex, race, married and female, and geographic region.

Table 2: Respondent Demographic Characteristics

Characteristic	No or Minimal Depression n=121,093,270	Moderately Severe to Severe Depression n=37,974,900	p Value
Male, %	53.40	47.51	0.054
Female, %	46.60	52.49	
White, %	76.92	75.10	0.482
Other, %	11.56	13.99	
Black, %	11.52	10.91	
Hispanic origin, %	7.94	16.21	< 0.001
Married and male, %	29.26	20.09	0.002
Married and female, %	23.57	20.68	0.217
Age, mean (SD)	50.17 (16.90)	39.80 (14.12)	< 0.001
18 - 44 years old, %	39.83	61.44	< 0.001
45 - 64 years old, %	36.05	34.25	
≥ 65 years old, %	24.13	4.31	
Education			
High school or less, %	42.66	56.69	< 0.001
Associate or bachelor, %	41.87	33.31	0.005
Graduate degree, %	15.48	10.00	0.013
Employment			
Employed full-time, %	38.03	33.39	< 0.001
Employed part-time, %	12.36	14.18	
Not employed, looking, %	10.41	20.39	
Not employed, not looking,%	39.20	32.04	
Insurance - Yes, have insurance, %	89.72	81.77	< 0.001
Region			
Northeast, %	18.76	15.89	0.504
Midwest, %	21.38	20.04	
South, %	36.24	38.34	
West, %	23.63	25.73	

Clinical characteristics are presented for the two groups in Table 3. Individuals in the MSS group reported more insomnia symptoms (difficulty initiating sleep, difficulty maintaining sleep, and non-restorative sleep) when compared to the NMD group (47.32% vs. 4.9%, $p < 0.05$), 53.93% vs. 9.53%, $p < 0.05$, 77.16% vs. 47.08%, $p < 0.05$, respectively). Sleep apnea was reported more frequently in the MSS group vs. the NMD group (17.32% vs. 7.47%, $p < 0.05$). Significantly more respondents in the MSS group compared to the NMD group had mild to moderate anxiety (42.05% vs. 10.72%, $p < 0.05$) and severe anxiety (55.30% vs. 0.42%, $p < 0.05$). However, there was a higher percent of individuals with no or minimal anxiety in the NMD vs. MSS groups (88.86% vs. 2.65%, $p < 0.05$). The percentage of respondents with an alcohol or drug problem was greater with the MSS vs. NMD group (10.82% vs. 2.28%, $p < 0.05$).

Additional comorbidity group differences were observed between MSS and NMD for kidney disease (3.38% vs. 1.11%, $p < 0.05$), asthma/COPD (18.73% vs. 9.48%, $p < 0.05$), overactive bladder (8.13% vs. 2.84%, $p < 0.05$), migraine or severe headaches (27.29% vs. 11.93%, $p < 0.05$), multiple sclerosis (1.72% vs. 0.41%, $p = 0.012$), fibromyalgia (7.10% vs. 1.90%, $p < 0.05$), and obesity (35.26% vs. 26.24%, $p = 0.001$).

There were no comorbidity between group differences for cancer, hypertension, hyperlipidemia, diabetes mellitus, osteoarthritis, hypothyroidism, or gout.

Table 3: Respondent Clinical Characteristics

Characteristic	No or Minimal Depression n=121,093,270	Moderately Severe to Severe Depression n=37,974,900	p Value
Insomnia symptoms			
Difficulty initiating sleep, %	4.90	47.32	< 0.001
Difficulty maintaining sleep, %	9.53	53.93	< 0.001
Nonrestorative sleep, %	47.08	77.16	< 0.001
Kidney disease, %	1.11	3.38	0.007
Cancer, %	3.96	2.91	0.368
Sleep apnea, %	7.47	17.32	< 0.001
High blood pressure (hypertension), %	29.95	31.79	0.511
High cholesterol (hyperlipidemia), %	26.51	21.58	0.068
Type 2 diabetes mellitus, %	10.70	9.92	0.695
Asthma or COPD, %	9.48	18.73	< 0.001
Overactive bladder, %	2.84	8.13	< 0.001
Osteoarthritis, %	9.36	8.60	0.658
Migraines or severe headaches, %	11.93	27.29	< 0.001
Multiple sclerosis, %	0.41	1.72	0.012
Anxiety symptoms			
No or minimal anxiety (GAD-7 $\leq$ 5), %	88.86	2.65	< 0.001
Mild to moderate anxiety (GAD-7 6-14), %	10.72	42.05	< 0.001
Severe anxiety (GAD-7 $\geq$15), %	0.42	55.30	< 0.001
Alcohol or drug problem, %	2.28	10.82	< 0.001
Hypothyroidism, %	5.75	6.48	0.584
Fibromyalgia, %	1.90	7.10	< 0.001
Gout, %	2.75	2.11	0.512
Obesity, %	26.24	35.26	0.001

Table 4 includes the results of the multivariate logistical model utilized to evaluate the respondent demographic and clinical factors associated with moderately severe to severe depression. When controlling for the different variables, the insomnia symptoms of difficulty initiating sleep, maintaining sleep and nonrestorative sleep were all

significantly associated with moderately severe to severe depression (OR=5.20, 95% CI: 3.10-8.74, $p < 0.05$, OR=4.16, 95% CI: 2.66-6.52, $p < 0.05$, OR=1.89, 95% CI: 1.37-2.61, respectively). Respondents with anxiety had a higher odds of reporting moderately severe to severe depression (OR=4.55, 95% CI: 3.13-6.62, $p < 0.05$). Two additional comorbidities (kidney disease and hypertension) were also predictive of more severe depression (OR=6.36, 95% CI: 2.45-16.48, $p < 0.05$, OR=1.57, 95% CI: 1.05-2.36, $p = 0.03$), respectively).

The following factors were associated with a lower odds of reporting moderately severe to severe depression: age (OR=0.94, 95% CI: 0.93-0.96, $p < 0.05$), married and female (OR=0.63, 95% CI: 0.40-0.99, $p = 0.04$), and insurance status (OR=0.51, 95% CI: 0.33-0.79, $p = 0.002$).

Table 4: Factors Associated with Moderately Severe to Severe Depression

Factor	β	Adjusted Odds Ratio	95% Confidence Interval		p Value
			Lower	Upper	
Sex	0.275	1.32	0.86	2.03	0.210
Race (White)	-0.067	0.94	0.64	1.37	0.730
Married and male	0.181	1.20	0.70	2.04	0.506
Married and female	-0.459	0.63	0.40	0.99	0.044
Age	-0.057	0.94	0.93	0.96	< 0.001
Degree status	-0.158	0.85	0.58	1.25	0.417
Graduate degree status	-0.077	0.93	0.51	1.68	0.800
Employment full-time	-0.151	0.86	0.59	1.24	0.423
Northeast	-0.224	0.80	0.50	1.27	0.347
Midwest	-0.033	0.97	0.62	1.50	0.884
West	0.262	1.30	0.84	2.01	0.242
Insurance status	-0.682	0.51	0.33	0.79	0.002
Insomnia symptoms					
Difficulty initiating sleep	1.649	5.20	3.10	8.74	< 0.001
Difficulty maintaining sleep	1.427	4.16	2.66	6.52	< 0.001
Nonrestorative sleep	.635	1.89	1.37	2.61	< 0.001
Kidney disease	1.849	6.36	2.450	16.48	< 0.001
Cancer	-0.031	0.967	0.44	2.12	0.937
Sleep apnea	0.434	1.54	0.90	2.66	0.117
Hypertension	0.451	1.57	1.05	2.36	0.029
Hyperlipidemia	-0.134	0.88	0.54	1.42	0.585
Type 2 diabetes mellitus	0.254	1.29	0.660	2.52	0.457
Asthma of COPD	0.176	1.19	0.734	1.94	0.477
Overactive bladder	0.579	1.78	0.870	3.66	0.114
Osteoarthritis	0.443	1.56	0.857	2.83	0.146
Migraine or severe headache	-0.010	0.99	0.64	1.53	0.964
Multiple sclerosis	1.414	4.11	0.84	20.02	0.080
Anxiety	1.516	4.55	3.13	6.62	< 0.001
Alcohol or drug problem	0.496	1.64	0.86	3.12	0.131
Hypothyroidism	-0.115	0.89	0.50	1.60	0.699
Fibromyalgia	0.760	2.14	0.76	5.99	0.148
Gout	-0.494	0.61	0.14	2.60	0.504
Obese	0.232	1.26	0.86	1.84	0.228

Discussion:

This study investigated the relationship between specific insomnia symptoms (difficulty initiating sleep, difficulty maintaining sleep, and nonrestorative sleep) and depression severity level in the US adult population. There are numerous factors that can contribute to a person's depression severity level; therefore, demographic, socioeconomic, and comorbidities were also included in the analyses. The clinical implication for this study was to aid clinicians in helping to determine whether specific insomnia symptom(s) within moderately severe to severe depression patients deserve further attention when developing a treatment plan.

There was a significantly higher percent of moderately severe to severe depression individuals who reported insomnia symptoms. Approximately 50% of patients within the MSS group reported difficulty falling asleep and/or difficulty maintaining sleep and 77.2% reported nonrestorative sleep. Sunderajan et al studied 3,743 patients diagnosed with major depressive disorder and reported that 84.7% had some type of insomnia symptoms defined as sleep onset, mid-nocturnal, or early morning.[11] Also, 27.3% of study participants presented with all three categories of insomnia symptoms. In another study, 687 participants were identified from the National Comorbidity Survey – Replication and evaluated to determine the impact of insomnia and hypersomnia in US adults with depression.[12] Insomnia and hypersomnia were prevalent in 27.7% of respondents with a previous major depressive episode. Among these respondents with a previous major depressive episode, 7.2% had no sleep problems, 59.1% had insomnia only, and 5.9% had hypersomnia only. The current study reports a higher percent of insomnia symptoms compared to the previously mentioned studies. This may be due to

the current study focusing on a more severe depression group as co-occurring insomnia symptoms have been associated with depression severity.[5,11,12]

Of particular interest is the high percent of respondents in both the NMD and MSSD groups who reported nonrestorative sleep. Previous studies have reported the prevalence of non-restorative sleep in the range of 25% - 36.5%.[13-15] However, among the published studies there are challenges when attempting to compare the number of individuals with nonrestorative sleep. The challenges stem from the use of varying definitions and different methodological approaches.[16] Despite these challenges, there is consistency with nonrestorative sleep being the most prevalent insomnia symptom.[13] Roth et all postulate that the prevalence may be indicative of nonrestorative sleep resulting from other insomnia symptoms (difficulty initiating sleep, difficulty maintaining sleep, early morning awakening) or as a distinct sleep problem.

When controlling for all other variables included in the univariate analyses, all three insomnia symptoms were predictors of moderately severe to severe depression. It is important to note that the PHQ-9 questionnaire that was utilized to stratify depression severity level does include the following sleep related item: trouble falling or staying asleep, or sleeping too much; therefore, the findings are consistent with difficulty initiating sleep and difficulty maintaining sleep being significantly associated with depression severity.[8] Taylor et al conducted a retrospective cross-sectional study including 772 community individuals which was designed to investigate the epidemiology of insomnia, depression, and anxiety.[5] As previously mentioned, an increase in insomnia frequency and the mean number of night awakenings were associated with increased depression severity scores as measured by the Beck Depression

Inventory. There was not a significant association between sleep onset latency, mean wake time after sleep onset, total sleep time, and sleep efficiency with depression. Another analysis examined the association between insomnia symptoms and depression severity was conducted with depressed patients enrolled in the STAR*D trial.[11] The authors concluded that the presence of insomnia symptoms was associated with greater depression severity. However, the authors did not report if specific insomnia symptoms were related to depression severity. Froese et al also investigated the relationship between insomnia symptoms and depression in an indigenous North American population.[6] Insomnia symptoms were independently associated with depression severity, but specific insomnia symptoms were not reported. Although there were published studies regarding the association between insomnia symptoms and depression severity, due to the difference in study methodologies and the lack of reporting specific insomnia symptoms it is difficult to compare results between studies.

In this study, nonrestorative sleep was also a significant predictor of moderately severe to severe depression. Sarsour et al completed a cross-sectional survey of 1,285 US health plan members with and without nonrestorative sleep symptoms.[17] Nonrestorative sleep was associated with depression and existed independently of other insomnia symptoms. Other studies support the presence of nonrestorative sleep in absence of other insomnia symptoms. Roth et al reported approximately one-third of individuals reported nonrestorative sleep in the absence of difficulty initiating sleep, difficulty maintaining sleep, or early morning awakening.[13] Another study examined the characteristics of nonrestorative sleep by utilizing both objective sleep measures (polysomnography) and questionnaires.[18] The authors concluded that nonrestorative sleep could occur in the

absence of other insomnia symptoms. In addition to occurring independently of other insomnia symptoms, nonrestorative sleep can also have a negative impact on daytime impairment and increase the number of physician visits.[19] Despite the independence and negative consequences associated with nonrestorative sleep, difficulty initiating sleep and difficulty maintaining sleep remain the focus of treatment with nonrestorative sleep remaining as an elusive target.[18]

The remaining predictors of moderately severe to severe depression were younger age (positive association), being married and female (negative association), insurance coverage (negative association), hypertension (positive association), kidney disease (positive association) and anxiety (positive association). In this study, approximately 60% of the moderately severe to severe depression respondents were in the 18 – 44 age range. A positive association between younger age and depression severity may be related to the higher reported prevalence of major depressive episode in the age ranges of 18-25 (10.5%) and 26-49 (7.4%).[20] Consistent with previous studies, marriage appeared to demonstrate a protective effect.[21,22] However, additional research needs to be conducted as to understand why this effect was seen in married women. The association between the lack of insurance coverage and depression severity may stem from these individuals not receiving treatment for their mental health issue.[23-25] Lastly, there have been numerous studies with consistent findings regarding the relationship between comorbidities (ex: hypertension, kidney disease, and anxiety) and depression.[9,21,26,27]

For the appropriate interpretation of the results, it is important to note the limitations of this study. Since this is a cross-sectional study it is unable to determine any type of causality between the variables included in the analyses. With this type of study design,

there could not be a determination of whether insomnia symptoms occurred before or after the depression symptoms. Symptoms were reported from individuals without any type of clinical review or objective data. Due to the lack of this additional information, it was unclear as to whether insomnia symptoms were impacting individuals during an acute episode, remission, or continuation phase. Another study limitation is that insomnia symptoms were evaluated as independent variables even though the PHQ-9 includes "trouble falling or staying asleep, or sleeping too much" as a depression severity assessment item. Insomnia symptoms (especially difficulty initiating or maintaining sleep) could be viewed as both independent and dependent variables. Previously published studies did not adequately address whether specific insomnia symptoms were associated with a higher level of depression severity. At study initiation, the nature of the association between specific insomnia symptoms and PHQ-9 scores was unclear. Although there were similar results when comparing the NHRS survey results to the US 2010 consensus, there is not a peer reviewed validation study. As a result of these limitations, further research is warranted to explore the relationship between specific insomnia symptoms and depression severity. In particular, a standard methodological approach is needed to characterize nonrestorative sleep symptoms.

Conclusions:

All three insomnia symptoms (difficulty initiating sleep, difficulty maintaining sleep, and nonrestorative sleep) were independently associated with depression severity. Of particular interest is the high percent of individuals reporting nonrestorative sleep which can occur in the absence of other insomnia symptoms; however, in clinical practice difficulty initiating sleep and maintaining sleep remain the focal point of treatment.

Increasing the awareness and consequences of all pertinent insomnia symptoms may aid clinicians in developing depression treatment plans tailored to the individual needs of each patient.

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