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Barbara Riegel

University of Pennsylvania, briegel@nursing.upenn.edu

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Abstract

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Methods: Data were collected from 266 subjects enrolled from three sites in the U.S. Sleep dysfunction was measured over the past month with the Pittsburgh Sleep Quality Index, using a score > 10 to indicate sleep dysfunction. Potentially modifiable clinical, behavioral, and psychological factors thought to be associated with sleep dysfunction were analyzed with hierarchical logistic regression analysis.

Results: When covariates of age, gender, race, data collection site, and New York Heart Association (NYHA) functional class were entered on the first step, only NYHA was a significant correlate of sleep dysfunction. When the clinical, behavioral, and psychological factors were entered, correlates of sleep dysfunction were the number of drugs known to cause daytime somnolence (OR = 2.08), depression (OR = 1.83), worse overall perceived health (OR = 1.64), and better sleep hygiene (OR = 1.40). Although most (54%) subjects had sleep disordered breathing (SDB), SDB was not a significant predictor of sleep dysfunction.

Discussion: Factors associated with sleep dysfunction in HF include medications with sleepiness as a side-effect, depression, poorer health perceptions, and better sleep hygiene. Sleep dysfunction may motivate HF patients to address sleep hygiene. Eliminating medications with sleepiness as a side-effect, treating depression and perceptions of poor health may improve sleep quality in HF patients.

Keywords

Heart failure, sleep, sleep dysfunction, self-rated health, medications, sleep hygiene, depression

Disciplines

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Modifiable Factors Associated with Sleep Dysfunction in Adults with Heart Failure

Barbara Riegel, DNSc, RN, FAAN, FAHA [Professor],
University of Pennsylvania School of Nursing

Dale Glaser, PhD [Principal—Glaser Consulting],
San Diego, CA Adjunct Associate Professor of Statistics, University of San Diego School of Nursing

Kathy Richards, PhD, RN, FAAN [Professor],
University of Pennsylvania School of Nursing

Steven L. Sayers, PhD [Associate Professor],
University of Pennsylvania School of Medicine and Philadelphia Veterans Affairs Medical Center

Amy Marzolf, RN [Heart Failure Nurse Coordinator],
Heart Failure and Transplant Center, University of Pennsylvania

William S. Weintraub, MD [Chief of Cardiology], and
Director of Christiana Care Center for Outcomes Research Christiana Care Health System, Newark, DE

Lee R. Goldberg, MD, MPH [Associate Professor]
University of Pennsylvania School of Medicine

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Corresponding Author: Dr. Barbara Riegel, Professor, School of Nursing, University of Pennsylvania, 418 Curie Boulevard, Philadelphia, PA 19104-4217, 215-898-9927 (W), 240-282-7707 (eFAX), briegel@nursing.upenn.edu.

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Keywords

heart failure; sleep; sleep dysfunction; perceived health; medications; sleep hygiene; depression

Introduction

Heart failure (HF) remains a persistent contributor to frequent hospitalizations, high mortality, and escalating health care costs.^{1 2} Quality of life is worse for HF patients than the general population, patients with other chronic diseases, and patients with other cardiac diseases (e.g., myocardial infarction).³⁻⁵ Poor sleep quality is also common in adults with HF. Several investigators have shown that poor sleep quality is a contributor to poor quality of life in adults with HF.⁶⁻⁹

Sleep dysfunction has been defined as encompassing the domains of insomnia, sleep adequacy, and somnolence.¹⁰ The focus of this study is on sleep adequacy, defined as difficulty in initiating or maintaining sleep.¹¹ There is surprisingly little research describing the factors associated with sleep adequacy in adults with HF. Therefore, the purpose of this study was to identify the factors associated with self-reported sleep dysfunction. If mild, sleep dysfunction may not impair social or occupational functioning, although it may cause feelings of restlessness, irritability, mild anxiety, daytime fatigue, and tiredness.¹¹ Moderate vs. severe sleep dysfunction is a matter of degree; complaints of relatively less sleep are typically accompanied by increasing complaints of daytime dysfunction.

Sleep dysfunction is common in adults. In a cross-sectional study of 25,579 adults from France, the U.K., Germany, Italy, Portugal, Spain and Finland, 34.5% of the sample reported difficulty initiating or maintaining sleep or non-restorative sleep at least 3 nights per week.¹² In a random sample of 4,885 adults from just the U.K., 37% reported sleep dysfunction.¹³ In the 2002 National Health Interview Survey (NHIS), an annual in-person survey of the civilian, non-institutionalized U.S. population, only 17.4% of 31,044 adults reported trouble sleeping.¹⁴ But in the 2002 Sleep in America poll, complaints of difficulty falling asleep, waking a lot during the night, waking up too early and not being able to get back to sleep, and waking up feeling unrefreshed were reported by 58% of respondents; 35% reported at least one of these four symptoms of sleep dysfunction every night or almost every night in the past year.¹⁵ Sleep dysfunction is more common in elders,^{13 16} although significant variability exists.¹⁷ For unknown reasons, sleep dysfunction is more prevalent in females than males, regardless of age.¹⁵

Sleep dysfunction is also a common complaint of chronically ill patient populations. In a cohort (n=3,445) of patients with hypertension, diabetes, HF, myocardial infarction, and/or depression, 16% had severe insomnia and 34% had mild insomnia. Sleep dysfunction was most common in individuals with a diagnosis of depression, HF, obstructive airway disease, back, hip, or prostate problems.¹⁸

Few investigators have studied sleep dysfunction in adults with HF. In one sample of 223 adults with HF, 36% reported not getting enough sleep.⁷ The factor interfering the most with sleep was nocturia; 90% of the men and 80% of women reported nocturia. Anxiety (22%) and nocturnal ruminations (16%) were also common. In an earlier study from the same group, 20 HF patients (13 men) reported that their sleep was affected by demands of daily

activities and the disease itself, in addition to cardiac symptoms such as nocturnal dyspnea, cough, and palpitations.¹⁹ Interestingly, although the severity of sleep disordered breathing (SDB) is positively associated with objective evidence of sleep quality and efficiency, SDB is not necessarily associated with subjective complaints of sleep dysfunction or excessive daytime sleepiness.^{20 21}

In summary, although sleep dysfunction appears to be common in older adults with chronic illness and sleep problems are associated with poor quality of life in the HF population, few investigators have described the factors causing sleep dysfunction in adults with HF. Thus, we remain uncertain exactly how prevalent sleep dysfunction is in HF patients and what causes their difficulties in initiating and maintaining sleep. Without such knowledge, the ability to design interventions to improve sleep is limited to addressing specific symptoms in individual patients. Thus, we sought to identify the factors associated with self-reported symptoms of sleep dysfunction in a large sample of adults with HF, focusing on factors that are potentially modifiable with the intention of designing an intervention.

Methods

The methods used in this study have been reported previously,²² but in brief, a cross-sectional observational design was used to analyze data from a consecutive sample of 266 adults with HF who were enrolled from three outpatient settings in Philadelphia, Pennsylvania and Newark, Delaware. The local Institutional Review Board of each site approved the study. All subjects provided informed consent. Research assistants collected data during home visits. Clinical information was abstracted from the medical record by registered nurses. This analysis used data collected between 2007 and 2009.

Individuals were included in the study if they had chronic Stage C HF confirmed through a review of the medical record. Patients with both systolic (left ventricular ejection fraction < 40%) and preserved left ventricular systolic function (diastolic HF) were included. Participants had to have visual acuity sufficient to read the study materials, hearing sufficient to engage in a dialogue, and be fluent in English. Exclusion criteria were working nights or rotating shifts, major depression, significant cognitive impairment, stage 5 chronic kidney disease, an imminently terminal illness, plans to move out of the area, or a recent history of serious drug or alcohol abuse. Institutionalized individuals were excluded because the primary goal of the study was to explore the effect of sleep problems on the ability to perform self-care; institutional individuals are not usually responsible for independent self-care. Cognitive impairment was screened using the Telephone Interview of Cognitive Status (TICS);²³ anyone with a score <24 was excluded. This cut-point was chosen to accommodate a broad range of HF patients, many of whom have mild cognitive impairment (TICS score of 21–25).²⁴ Major depression was screened in the medical record. Patients noted to have severe depressive illness were not contacted. In addition, all consenting patients were further screened with the Patient Health Questionnaire (PHQ-9).²⁵ We excluded individuals reporting 5 or more of the 9 symptoms on the PHQ-9 more than half the days in the past 2 weeks; 1 of the symptoms had to be depressed mood or anhedonia. For those who passed screening, we continued to use data from a subset of the PHQ-9, the PHQ-2, to measure mild depressive symptoms.

In this analysis we explored potentially modifiable clinical, behavioral, and psychological factors thought to be associated with sleep dysfunction. These factors were chosen based on clinical experience with this population and on published literature describing factors associated with sleep dysfunction. Clinical factors tested were number of prescription medications²⁶ and the number of drugs known to cause daytime somnolence,²⁷ quality of the treatment regimen,²⁸ systolic blood pressure,²⁹ obesity,³⁰ clinical factors that disturb

sleep such as pain,¹⁸ and the presence and severity of SDB.²⁷ Systolic blood pressure was included because short sleep duration is associated with high blood pressure.²⁹ Waist circumference was used because it is thought to be a more sensitive indicator of obesity than body mass index.³¹ Behavioral factors included exercise,²⁶ alcohol use,^{26 27} smoking,²⁶ and sleep hygiene measures.³² Psychosocial factors included depressive symptoms,¹⁸ perceived overall health,³³ and social support.²⁶

Measurement

Sleep dysfunction was measured over the past month using the Pittsburgh Sleep Quality Index (PSQI).³⁴ The PSQI measures the domains of subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each subscale was scored 0 (not in the past month) to 3 (three or more times a week) and added to produce the sleep dysfunction score. Internal consistency of the full 19 item PSQI is usually in the range of 0.77 to 0.83;³⁴ reliability of the PSQI was 0.73 in this study. A score of >10 was used to classified participants as having sleep dysfunction.³⁵

The medication information used in testing the model was obtained by research assistants (RAs) who reviewed medicine bottles, interviewed subjects about their medicines, or reviewed medicine lists to obtain information on all prescription and over-the-counter medicines taken by participants. All drugs prescribed by a licensed provider were included in the number of prescription medications, even if the drug was obtainable over-the-counter (e.g., antihistamines). Each drug listed was compared to a detailed list of drugs associated with daytime somnolence to identify the number of medicines taken that are known to sleep dysfunction. Quality of the treatment regimen was judged by registered nurses using performance standards devised from the 2006 Heart Failure Society of America Comprehensive HF Guidelines, the most up-to-date clinical guidelines in place at the time.³⁶ The proportion (0 – 100%) of evidence-based treatments prescribed was used in analysis. Blood pressure was measured by the RAs using standardized procedures.³⁷ Waist circumference was measured as specified by the National Heart, Lung and Blood Institute (http://www.nhlbi.nih.gov/guidelines/obesity/e_txtbk/txgd/4142.htm).

A physician-diagnosis of sleep disordered breathing (SDB) based on polysomnography was obtained from the medical record at the time of enrollment. If no documentation of recent sleep testing was found in the medical record, sleep was assessed in the home using an unattended sleep study device, the Embletta (Medcare, Buffalo, NY). The Embletta is a pocket-sized digital recorder that provides data on position and activity, leg movement, oxygen saturation, pulse, oral flow, snoring, and respiratory effort. The Embletta software is known to overestimate the apnea-hypopnea index (AHI),³⁸ so rather than using AHI from these two different sources in the analysis, the AHI was dichotomized. Individuals with an AHI \geq 5 were considered to have SDB.³⁹

Exercise frequency, alcohol use, and smoking behavior were collected as self-report data. Sleep hygiene behaviors such as keeping a routine bedtime and engaging in relaxing activities prior to sleep were scored on a 0 (never) to 3 (every night) scale, with higher scores indicating better sleep hygiene. The raw score (range: 0 to 12) was used in analysis.

Depression was assessed using the two items in the PHQ-9 that focus on the classic symptoms of depression: depressed mood and anhedonia. The PHQ-2 has been used in other studies.⁴⁰ This abbreviated version was used because 3 items on the PHQ-9 address sleep and fatigue (i.e., trouble falling or staying asleep or sleeping too much; feeling tired or having little energy), introducing a confounding between cause and effect. Scores on the PHQ-2 range from 0 to 6, with higher scores indicating more depression. Perceived overall

health was measured using a single item from the Medical Outcomes Study:⁴¹ In general, would you say your health is poor, fair, good, very good, or excellent? Social support was assessed using the Multidimensional Scale of Perceived Social Support (MSPSS),⁴² a 12-item tool assessing support from family, friends, and a significant other. Total support scores were used in analysis. The reliability of this scale was reported to be 0.91 by the instrument authors. In this study, the alpha coefficient was 0.90.

Analysis

Standard descriptive statistics of central tendency and dispersion were used to characterize the sample of 266. A two-step hierarchical approach to multiple binary logistic regression was used to identify the best predictors of sleep dysfunction. Covariates used in analysis were age, gender, race, and data collection site. Others have noted that sleep dysfunction is more common in HF patients with worsening functional class,⁴³ so New York Heart Association (NYHA) functional class also was used as a covariate. Information needed to rate NYHA functional class was obtained with a standardized interview⁴⁴ and scored by a single board-certified cardiologist to avoid known issues with interrater reliability.⁴⁵

In the first step of the analysis, covariates were entered into the model. Then, the 13 variables theoretically anticipated to be associated with sleep dysfunction were entered in the second step. Chi-square analysis was used to determine if the set of clinical, behavioral, and psychosocial factors significantly improved model fit over and beyond the set of covariates. The Hosmer and Lemeshow test was assessed, noting that a nonsignificant result supports model fit. At the predictor level, the logit coefficients are reported for all of the explanatory variables, including odds ratios (OR) and the 95% confidence interval (CI) around the OR. Both sensitivity and specificity are reported. All analyses were conducted with the SPSS v. 18.0.2 software (Chicago, IL). An α of .05 was predetermined as the level of significance.

Results

The sample of 266 was predominately white (63%) and male (64%); mean age was 62 ± 12 years. Many subjects rated their health as fair or poor (54%). Only 12 individuals (4.5%) were not taking a medication known to be associated with sleepiness; 55.6% ($n = 148$) were taking 1 such medication but one subject was taking 7 such medicines. When a score of >10 on the PSQI was used to classify participants as having significant sleep dysfunction, 21.8% ($n = 58$) of the sample had sleep dysfunction (Table 1).

The slight majority of the sample ($n=151$, 54%) had SDB. Of these, only 75 (49.7%) had been treated with CPAP and of these, only 35 (47.3%) reported using it 6 hours per night in the past week. In univariate analysis, adjusting for continuous positive airway pressure (CPAP) use, SDB was not significantly associated with sleep dysfunction ($p=0.77$). The correlation between perceived health and depression measured with the PHQ-2 was only 0.19 ($p=0.002$).

When the covariates were entered at the first step, the model was significant ($\chi^2(7) = 25.35$, $p = .001$) and model fit was adequate ($\chi^2(8) = 13.13$, $p = .107$). At this initial step, the only significant covariate was NYHA ($p = .001$; OR = 2.06); a higher (worse) NYHA score was associated with twice the odds of having sleep dysfunction. Sensitivity was poor at this step (6.9%), but specificity was high (98.6%), with an overall accuracy of 78.6%.

At the second step, the addition of the 13 explanatory variables significantly improved model fit ($\chi^2(13) = 53.13$, $p < .05$). The Hosmer and Lemeshow test confirmed good model fit ($\chi^2(8) = 3.93$, $p = .864$). NYHA was no longer significant in the full model ($b = .454$, p

= .054). Significant correlates of sleep dysfunction were a higher number of drugs causing daytime somnolence, more depressive symptoms, worse perceived health, and better sleep hygiene. Sensitivity improved to 39.7% and specificity remained high (94.2%), with an overall accuracy of 82.3% (Table 2).

Discussion

The major findings of this study were that a higher number of drugs causing daytime somnolence, more depressive symptoms, and poorer overall perceived health increased the likelihood of having sleep dysfunction. Surprisingly higher sleep hygiene scores were associated with more sleep dysfunction in these patients, suggesting that HF patients may not bother with sleep hygiene until they have fairly significant sleep dysfunction. The model of covariates and 13 explanatory factors was specific (% of true negatives) but sensitivity (% of true positives) was low, suggesting that other important factors influence sleep dysfunction in adults with HF. Presumably many of the other factors associated with sleep dysfunction are not potentially modifiable and thus were not tested. Importantly, SDB was not a significant determinant of sleep dysfunction in this sample.

The finding that drugs with sleepiness listed as a common side-effect disrupt sleep is not really surprising but it does serve to remind clinicians to consider the side-effect profile of prescribed medications. A distressing number of people were taking such medications. It should be noted, however, that others have found little relationship between the medication profile of HF patients and sleep dysfunction.⁴⁶ The difference in results may be that we assessed the entire medication regimen, not just the cardiac medications prescribed to HF patients.

Other investigators have found a relationship between depression and sleep dysfunction in the general population as well as in those with HF.⁴⁷ Both the NIHS¹⁴ and the survey of adults with chronic illnesses¹⁸ described above noted the relationship between depression and sleep dysfunction. This is an important finding because major depression was an exclusion criterion and the vast majority of subjects had no depression or only minor depressive symptoms. Our results suggest that even mild depression is associated with sleep dysfunction.

Our finding that self-reported perceived health was a significant determinant of sleep dysfunction is interesting because this variable has been found previously to be associated with functional outcomes,^{48 49} health care utilization,⁵⁰ and even mortality in other populations.^{51 52} In a sample of HF patients, those with poor perceived health were more likely to be hospitalized over a 12 week period.⁵³ Others have found that perceived health was an independent predictor of cardiovascular mortality and HRQL in elders with HF.^{54 55} Further, perceived health is commonly unrelated to health as rated by a physician. For example, 17% to 21% of prior samples have been shown to perceive themselves to be in poor health, despite objectively good physical health.^{56 57} The manner in which health perceptions influence sleep dysfunction is unclear and requires further research.

Another interesting finding was that better sleep hygiene was associated with more sleep dysfunction. As this was cross-sectional data, we suspect that the patients were devoting relatively more effort to basic sleep hygiene measures because of the sleep dysfunction.

Functional status was associated with sleep dysfunction in the first step of the analysis, with a trend remaining after the 13 predictors were added to the model. Finding NYHA to be associated with sleep quality was not surprising, as Principe-Rodriguez and colleagues previously found that worse NYHA was associated with insomnia.⁴³ The sleep disruption associated with functional status may reflect nocturnal fluid shifts.

Although it may appear counterintuitive that SDB was not associated with sleep dysfunction, this finding is similar to that of other investigators.^{58 59} For example, Johansson and colleagues⁶⁰ found that only difficulty initiating sleep was associated with SDB. In another population of patients referred for polysomnography, most (54.9%) reported sleep dysfunction.⁶¹ There was no association between sleep dysfunction and SDB, however. In fact, sleep dysfunction was more common in patients without SDB, which the authors speculated may reflect coexisting factors such as psychiatric disorders and chronic pain.

We suspected that a variety of other factors would be associated with sleep dysfunction, but none of those factors was a significant determinant of sleep dysfunction in this sample. For example, the NHIS found that hypertension and obesity were associated with sleep dysfunction,¹⁴ which we did not find in the current study. The survey of adults with chronic conditions discussed above¹⁸ found no significant trends for smoking status, alcohol use, or body mass index in relation to sleep dysfunction, as we found.

Limitations of this study include that the diagnosis of SDB was obtained from the medical record on many of the subjects and those with a previous diagnosis of SDB as well as those with a new diagnosis established as a part of the study were combined in these analyses. However, as only confirmed diagnoses of SDB were used and those in doubt were validated with a home sleep study, this is not seen as a major limitation. Finally, although the quality of the treatment regimen was scored as a proportion, relatively few treatments are advocated in the clinical guidelines for preserved systolic function, so the scores for that group could be inflated.

In summary, the results of this study have provided a set of potentially modifiable contributors to acute insomnia in adults with HF including use of medicines known to cause somnolence, depression, and perceptions of poor health. Our next step will be to design and test an intervention intended to decrease sleep dysfunction by addressing the medication regimen, depression, and health perceptions, with the goal of potentially improving outcomes in this large and growing patient population.

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Table 1

Characteristics of the sample overall. Mean \pm standard deviation or n (%) is reported.

	Sample (n=266)
Age (years)	62 \pm 12
Male	171 (64)
Race/Ethnicity	
White	163 (63)
Black	89 (33)
Other	9 (3.4)
Education	
Less than high school	26 (9.8)
High school	95 (36)
At least some college	145 (54)
Household Income	
Comfortable	94 (35)
Enough to make ends meet	128 (48)
Not enough to make ends meet	44 (16)
Smoking	
Current	29 (11)
Former	148 (56)
Never	89 (33)
Body mass index (BMI) (kg/m ²)	30.9 \pm 7.99
Waist circumference in centimeters	107 \pm 19
Exercise	
None or <30 minutes/week	103 (39)
30 minutes to 3 hours/week	115 (43)
>3 hours/week	48 (18)
Average Alcohol Use	
Never	139 (52)
Rarely (1-2 drinks/week)	90 (34)
2-7 drinks per week	28 (10)
Heavy (8 or more drinks per week or 5+ occasions)	9 (3)
Perceived overall health	
• Excellent/Very Good	30 (11)
• Good	92 (35)
• Fair	111 (42)
• Poor	33 (12)

	Sample (n=266)
Systolic blood pressure (mmHg)	116 ± 18
Years with heart failure	6.2 years
Months with heart failure	74 ± 72 mo
Ejection fraction (%)	36 ± 17
Heart failure type	
• Systolic/mixed	213 (80)
• Diastolic	52 (20)
• Unspecified ²	1 (0.4)
Charlson Comorbidity Categories	
• Low	141 (53)
• Moderate	95 (36)
• High	30 (11)
NYHA functional class	
• Class I & II	58 (22)
• Class III	159 (60)
• Class IV	49 (18)
Sleep Study	
• Prior polysomnography	175 (66)
• Embletta testing during the study	91 (34)
Sleep Disordered Breathing (SDB)	143 (54)
• Treated with CPAP	76 (27)
Number of prescription medications	9.8 ± 4.0
Angiotensin-Converting Enzyme (ACE) inhibitor	156 (59)
Angiotensin II Receptor Blocker (ARB)	76 (29)
Diuretic	214 (80)
Beta-Blocker	245 (92)
Number of medications known to cause daytime somnolence	1.56 ± .98
Quality of the treatment regimen	.84 ± .21
Depressive symptoms score (PHQ-2)	.79 ± 1.04
Insomnia score	4.43 ± 3.08
Sleep Hygiene score	2.09 ± 1.95
MSPSS total support score	72 ± 12

NYHA = New York Heart Association; PHQ-2 = Patient Health Questionnaire, 2 items CPAP = Continuous positive airway pressure, MSPSS = Multidimensional Scale of Perceived Social support

Table 2

Hierarchical Multiple Logistic Regression (n = 266)

Step 1-Covariates	b	SE	p	OR	95% CI (OR)
age	-.022	.014	.109	.979	.953, 1.01
gender	-.338	.365	.354	.713	.348, 1.46
race (Black vs. White)	.172	.347	.621	1.187	.601, 2.34
race (Other vs. White)	-.641	1.106	.562	.527	.060, 4.60
site (site 3 vs. 1)	-.066	.438	.879	.936	.397, 2.21
site (site 2 vs. 1)	.530	.473	.262	1.699	.673, 4.29
NYHA functional class	.721	.210	.001	2.057	1.364, 3.10
Step 2-Predictors					
age	-.019	.017	.248	.981	.949, 1.01
gender	-.350	.460	.447	.705	.287, 1.74
race (Black vs. White)	.154	.474	.746	1.166	.461, 2.95
race (Other vs. White)	-1.013	1.236	.412	.363	.0322, 4.09
site (site 3 vs. 1)	-.434	.538	.420	.648	.226, 1.86
site (site 2 vs. 1)	.383	.585	.513	1.467	.466, 4.62
NYHA functional class	.454	.236	.054	1.575	.992, 2.50
Total number of prescription drugs	-.033	.062	.589	.967	.857, 1.09
Number of Drugs Cause Daytime Somnolence	.733	.233	.002	2.082	1.33, 3.29
Treatment quality score	.402	.958	.674	1.496	.229, 9.77
Systolic blood pressure	-.019	.011	.089	.982	.961, 1.00
Waist circumference	-.002	.012	.863	.998	.976, 1.02
Sleep Disordered Breathing	.084	.413	.839	1.088	.484, 2.45
Exercise	-.186	.131	.155	.830	.642, 1.07
Alcohol consumption	-.297	.260	.253	.743	.447, 1.24
Smoking history	-.424	.298	.155	.654	.365, 1.17
Sleep hygiene	.334	.103	.001	1.397	1.14, 1.71
Depression (PHQ-2)	.602	.177	.001	1.827	1.29, 2.59
Perceived overall health	.495	.241	.040	1.641	1.02, 2.63
MSPSS total social support score	.006	.016	.710	1.006	.975, 1.04

Note: b = logit; parameter estimates derived from each step

OR = Odds Ratio

MSPSS = Multidimensional Scale of Perceived Social Support; PHQ-2 = Patient Health Questionnaire