

## Napping, Nighttime Sleep, and Cardiovascular Risk Factors in Mid-Life Adults

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**Study Objectives:** To evaluate the relations between sleep characteristics and cardiovascular risk factors and napping behavior, and to assess whether daytime napping leads to subsequent better or worse sleep.

**Methods:** The sample consisted of 224 (African American, Caucasian, and Asian) middle-aged men and women. Sleep measures included nine nights of actigraphy and sleep diaries, sleep questionnaires, and one night of polysomnography to measure sleep disordered breathing.

**Results:** More frequent napping was associated with shorter nighttime sleep duration averaged across the nine nights of actigraphy (especially among African Americans), more daytime sleepiness, more pain and fatigue by diary, and increased body mass index and waist circumference. Shorter nighttime sleep duration

was associated with taking a nap during the next day and taking a nap was associated with less efficient sleep the next night.

**Conclusions:** Napping in middle-aged men and women is associated with overall less nighttime sleep in African Americans and lower sleep efficiency as measured by actigraphy, and increased BMI and central adiposity. These findings point to the importance of measuring of napping in understanding associations of sleep with cardiovascular risk.

**Keywords:** Actigraphy, napping, obesity, cardiovascular risk factors

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Epidemiologic studies consistently report increased risk of cardiovascular morbidity and mortality among persons who report short or long sleep duration.<sup>1</sup> These studies have primarily focused on duration of nighttime sleep and have not independently considered potential benefits or risks associated with napping during the day. Napping may be beneficial, especially among short sleepers. Consistent with that interpretation are the results of a longitudinal study in Greece where frequent siesta takers had reduced cardiac mortality over a 6-year follow-up period.<sup>2</sup> On the other hand, survivors of myocardial infarction reported taking more frequent and longer siestas, compared to healthy controls.<sup>3</sup> In two longitudinal studies of elderly persons, all-cause, cancer, and cardiovascular disease mortality rates were higher among persons reporting longer daytime naps.<sup>4,5</sup>

The prevalence of napping reported in surveys and in diaries ranges from approximately 10% to 65%.<sup>6</sup> People who report frequent napping tend to be older and report poorer health/functional status<sup>7,9</sup> and more sleep problems,<sup>7,9</sup> suggesting that napping may be a consequence of poor sleep and/or poor health. In a prospective study of elderly women, women who reported napping on a daily basis have elevated risk for cardiovascular and all-cause mortality over 7 years of follow-up.<sup>10</sup> In another elderly sample, Goldman, et al., reported that taking a longer nap during the day was associated with shorter sleep the next night as determined by actigraphy.<sup>11</sup> In contrast to the largely negative associations between habitual napping and general health, short-term laboratory studies generally report positive

### BRIEF SUMMARY

**Current Knowledge/Study Rationale:** There is little information on ethnic differences in the relationship of napping behavior and nighttime sleep measured objectively. We conducted this study of actigraphy measured nighttime sleep and self-reported napping in an ethnically diverse sample of middle-aged men and women.

**Study Impact:** The findings of the study identify the association of napping behavior and cardiovascular risk factors, and of napping on subsequent night's sleep. Differences in sleep duration related to napping may increase cardiovascular risk for certain ethnic groups.

effects of a nap on neurobehavioral functions, such as alertness,<sup>12</sup> cognitive performance,<sup>13</sup> and memory.<sup>14</sup>

The purpose of our investigation was three-fold. First, we tested whether daytime napping was associated with objective and self-reported sleep characteristics measured by actigraphy, sleep diaries, and sleep questionnaires. Secondly, using actigraphy, we investigated the serial relationships between napping and nighttime sleep, i.e., whether daytime napping was associated with better or worse sleep the subsequent night and/or whether short or disturbed sleep was associated with napping the subsequent day. Thirdly, we tested whether frequent napping was associated with known cardiovascular risk factors, specifically obesity, elevated blood pressure, and physical inactivity. Finally, because the sample was multiethnic, and ethnicity is a correlate of both sleep and cardiovascular risk,<sup>15,16</sup> we also explored whether the associations varied by race/ethnicity.

## METHODS

### Participants

Participants in the study were recruited from a study called Heart Strategies Concentrating on Risk Evaluation (HeartSCORE), an ongoing prospective/nested intervention study at the University of Pittsburgh, Pittsburgh, PA.<sup>17</sup> HeartSCORE was designed to identify the impact of nontraditional cardiovascular risk factors in 2,000 African American, Caucasian, and Asian men and women in western Pennsylvania. A subset of participants from HeartSCORE was recruited for the current study, called Sleep Strategies Concentrating on Risk Evaluation (SleepSCORE). Exclusionary criteria included pregnancy, treatment for sleep disordered breathing, nighttime work schedule, regular use of medication for sleep or diabetes, and a history of myocardial infarction, interventional cardiology procedures, or stroke. Individuals on antihypertensive medication were not excluded. Eligible persons enrolled in HeartSCORE were approached to determine their interest in participating in SleepSCORE. The final sample was composed of 224 persons (113 men and 111 women between the ages of 45-78), including 123 Caucasians, 4 Asians, and 97 African Americans.

### Overview of Protocol

The SleepSCORE protocol began within approximately 3 months of a HeartSCORE visit. The 10-day protocol for SleepSCORE included the following: daily wrist actigraphy and daily sleep diary entries in the morning and evening; 2 nights of in-home polysomnography (PSG), with sleep disordered breathing measured on the first night of the protocol; 48 hours of ambulatory blood pressure monitoring; 2 overnight urine collections for catecholamines; and completion of psychosocial questionnaires. Resting blood pressure was determined at a laboratory visit immediately prior to the beginning of the ambulatory blood pressure portion of the protocol. The Institutional Review Board of the University of Pittsburgh reviewed and approved the protocol, and all participants signed informed consent prior to beginning the protocol. Participants received financial remuneration for their participation as well as detailed reports of their PSG sleep and ambulatory daytime and nighttime blood pressure. A complete description of the protocol can be found elsewhere.<sup>15</sup>

### Measurement of Sleep

#### Sleep Diary Measures

Participants completed a sleep diary in the evening before going to bed and upon awakening in the morning. The diary, a modification of the Pittsburgh Sleep Diary,<sup>18</sup> is a daily record of sleep-wake timing, sleep quality, mood and physical symptoms, napping, exercise, substance and medication use, and factors that interrupted nighttime sleep. On the evening diary, participants were asked to indicate the *total number of minutes* they napped during that day. Persons who reported 0 minutes of napping on every day of the protocol were considered to be non-nappers. The time a person reported in the sleep diary as “trying to go to sleep” was considered bed time, and the time they “fi-

nally awoke for the day” was considered wake time. In addition, they rated the extent to which they experienced discomfort or pain during the night on a scale of 0-4. They also rated the extent to which they felt fatigue or pain/discomfort during that day, from “not at all” to “extremely” on a scale of 0-4.

#### Actigraphy

Participants wore the Actiwatch 16 (Phillips Respironics, Bend, OR) from day 1 to day 10 of the protocol. Data were collected in 1-min epochs using the default (medium) threshold for detection of wake and sleep periods. Bedtime and wake time from the sleep diary were used to define the sleep period from which the actigraphy calculated sleep variables. Stored data were downloaded into the Actiware software program (version 3.3) for statistical analysis of sleep measures including *nighttime sleep duration*: total minutes scored as sleep from sleep start to sleep end, *sleep latency*: total number of minutes from bedtime to sleep start, and *sleep efficiency*: total nighttime sleep duration divided by time in bed  $\times$  100. The Actiwatch has been widely used in research studies and the resulting sleep outcome measures have been validated against PSG measures.<sup>19,20</sup>

#### Sleep Questionnaires

The Pittsburgh Sleep Quality Index (PSQI) is a 19-item self-report questionnaire designed to measure sleep quality and quantity over the preceding month.<sup>21</sup> Seven component scores are derived from the questionnaire that when totaled give a global score of overall subjective sleep quality ranging from 0 to 21, with higher scores indicative of poorer sleep quality and scores of  $\leq 5$  indicative of good sleep quality. The Epworth Sleepiness Scale (ESS) is an 8-item questionnaire designed to assess daytime sleepiness by determining the propensity of dozing or falling asleep during daytime activities.<sup>22</sup> Each question is rated as never to highly likely that one would fall asleep during that activity; scores are totaled to compute a total score ranging between 0 and 24 with scores  $> 10$  indicative of significant daytime sleepiness. We have previously reported that the PSQI and ESS measure independent constructs in this sample.<sup>23</sup>

#### Sleep Disordered Breathing

Sleep disordered breathing was measured on the first of 2 nights of polysomnography (PSG). Measures included nasal pressure and flow, respiratory effort using thoracic and abdominal bands, and oxygen saturation using fingertip oximetry. An apnea/hypopnea index (AHI) was calculated during nighttime sleep time using the American Academy of Sleep Medicine Task Force definitions.<sup>24</sup> Although AHI did not differ statistically across nap groups, it was used as a covariate in statistical analyses. Other than AHI data, PSG data were not included in data analyses because napping related to PSG could only be evaluated on 2 days of the 10 day/9 night protocol. Additional information regarding PSG sleep in this sample can be found elsewhere.<sup>15</sup>

#### Measurement of Cardiovascular Risk Factors

During a physical exam at the HeartSCORE visit, height, weight, and waist circumference were obtained by registered

nurses. Body mass index (BMI) was calculated by dividing weight in kilograms by height in centimeters squared. Usual level of physical activity was categorized by self-report as sedentary, mild, moderate, or strenuous. Resting blood pressure was determined by averaging 2 blood pressures taken after a seated rest period.

### Factors Related to Sleep and Napping

Age, race, gender, employment, and health status were determined by self-report. Perceived health status was rated by participants from poor to excellent on a 5-point scale. Because depression is associated with sleep quantity and quality, depressed mood was measured using the 20-item Center for Epidemiologic Studies Depression Scale (CES-D); the question regarding sleep quality was eliminated from the total score in analyses.<sup>25</sup> Self-report medical and medication history was also obtained. Use of medications affecting the cardiovascular system including antihypertensives, and use of antidepressants were not related to nap category. Nine categories of medical conditions were evaluated in relation to napping: cardiac, pulmonary, endocrine, gastrointestinal, nervous (neurologic disorders), mental (psychiatric disorders), kidney, cancer, and musculoskeletal. None of the self-report health conditions were significantly related to nap category.

### Data Analyses

The number of days that participants reported napping was summed across the protocol. Because the number of days of naps was not normally distributed, 4 nap frequency groups were formed: 0 naps, 1 nap, 2 or 3 naps, and  $\geq 4$  nap days over the 10-day protocol. Analyses of continuous dependent measures consisted of a 4-group analysis of covariance, with tests for linear trend. Covariates for continuous measures included age, race, gender, and depressive symptoms. Analyses of blood pressure, BMI, and central adiposity were conducted with and without AHI as a covariate. Analyses of categorical variables were based on  $\chi^2$  tests. We tested for interactions with race in all analyses and report below those that are significant. Mixed model analyses using actigraphy measures over 10 days determined, within subject, the association between daytime napping, nap length and the subsequent night's sleep, and the association between the previous night's sleep and napping the next day. Mixed model analyses included control for age, race, gender, depressive symptoms, and the previous night's sleep variable. Means are shown for both the transformed and non-transformed variables, although the analyses were conducted on the transformed data. Analyses excluding the 4 Asian participants did not alter the results, so the entire sample is included in this report. Two-tailed *p*-values  $< 0.05$  were considered statistically significant.

## RESULTS

Characteristics of the sample are shown in **Table 1**. The sample included approximately equal numbers of men and women; 43% were African American. The majority rated their health as at least "good," 9% were current smokers; and 10% reported engaging in strenuous physical activity. Twenty-nine percent reported no napping, 20% reported napping one day,

26% reported 2 or 3 days of napping, and 25% reported  $> 4$  days of naps over the 10 days of the protocol. Among those who reported any naps, the median number of nap days during the protocol was 2.5 days (IQR = 3), and the median nap length was 34.6 minutes (IQR = 35.6) per day of napping. There were no significant differences among nap categories in age, race, gender, employment, general health, physical activity, or smoking status. Depressive symptoms differed by group with those in the 2 highest nap groups reporting more symptoms compared to the 2 lowest groups.

### Relationships between Nap Groups and Daytime and Nighttime Sleep Characteristics

**Table 2** shows that the more frequent the napping the less nighttime sleep and the greater the self-reported daytime sleepiness, fatigue, and bodily pain. The association between napping frequency and nighttime sleep duration was only apparent among African American participants,  $p < 0.02$  for interaction with race. Sleep efficiency and sleep latency measured by actigraphy and overall sleep quality measured by the PSQI were not significantly associated with nap group ( $p$ 's  $> 0.10$ ). Mean AHI did not differ significantly between the 4 groups ( $p = 0.64$ ). Pain was significantly correlated with diary reports of daytime fatigue and daytime sleepiness ( $p$ 's  $< 0.05$ ). Except for nighttime sleep duration, there were no interactions with race.

### Within-Person Relationships between Napping and Nighttime Sleep

Mixed model analyses showed that taking a daytime nap, compared to not taking a daytime nap was associated with worse sleep efficiency ( $B = 0.061$ ,  $p = 0.02$ ) measured by actigraphy the subsequent night. Sleep efficiency on nights following a nap was 6.3% less efficient compared to nights not following a nap. There was no effect of taking a nap on sleep latency the subsequent night in the full sample. However, there was a significant interaction with taking a nap and race ( $p = 0.02$ ), such that taking a nap during the day was associated with longer sleep latency in African Americans only ( $B = 0.331$ ,  $p = 0.02$ ). Among African Americans there was a 39% greater sleep latency the subsequent night on a nap day compared to non-nap days. Taking a nap did not influence nighttime sleep duration the subsequent night.

Shorter nighttime sleep duration was related to taking a nap the following day ( $B = -0.286$ , O.R. 0.75, unit 1 hr,  $p < 0.0001$ ).

Comparable mixed model analyses were conducted regarding the length of a nap. Taking a longer nap on a given day did not affect subsequent sleep latency, sleep efficiency, or nighttime sleep duration. Shorter sleep duration was significantly associated with taking a longer nap the following day in the full sample ( $B = -1.77$ ,  $p = 0.001$ ). There was a significant interaction with race/ethnicity ( $p = 0.003$ ) with the effect of sleep duration being stronger in African Americans ( $p < 0.0001$ ) compared to Caucasians ( $p = 0.001$ ).

### Relationships Between Frequent Napping and Cardiovascular Risk Factors

**Table 3** shows the mean levels of waist circumference, BMI, and resting blood pressures. The more frequent the napping the

greater the waist circumference ( $p = 0.01$ ) and the greater the BMI,  $p = 0.004$ ) Blood pressure levels were not associated with nap frequency ( $p$ 's  $> 0.80$ ). The addition of AHI as a covari-

ate did not alter the results,  $p$  value for waist circumference  $p = 0.02$ , and for BMI  $p = 0.004$ . There were no interactions with race/ethnicity.

**Table 1**—Sample characteristics

Characteristic N = 224	Total Sample N = 224	0 naps N = 66	1 nap N = 44	2-3 naps N = 59	4 naps + N = 55	p-value
Age mean (SD)	59.9 (7.2)	60.1 (6.5)	58.2 (7.1)	59.7 (7.7)	61.5 (7.4)	0.18
Depressive Symptoms (CES-D) Mean (SD)	5.3 (6.6)	4.7 (7.1)	4.3 (6.3)	6.3 (5.9)	6.0 (6.8)	0.01
Race n (%)						
African American	97 (43.3)	31 (13.8)	15 (6.7)	21 (9.4)	30 (13.4)	0.11
Caucasian/Asian	127 (56.7)	35 (15.6)	29 (12.9)	38 (17.0)	25 (11.2)	
Gender n (%)						
Male	113 (50.4)	33 (14.7)	22 (9.8)	27 (12.1)	31 (13.8)	0.73
Female	111 (49.6)	29 (12.9)	22 (9.8)	32 (14.3)	24 (10.7)	
Employment n (%)						
Full-time	103 (46.0)	33 (14.7)	23 (10.3)	28 (12.5)	19 (8.5)	0.51
Part-time	33 (14.7)	8 (3.6)	5 (2.2)	10 (4.5)	10 (4.5)	
Retired	58 (25.9)	17 (7.6)	9 (4.0)	17 (7.6)	15 (6.7)	
Other	30 (13.0)	8 (3.6)	7 (3.1)	4 (1.8)	11 (4.9)	
General Health n (%)						
Excellent	42 (18.8)	17 (7.6)	9 (4.0)	11 (4.9)	5 (2.2)	0.11
Very good	81 (36.2)	22 (9.9)	18 (8.1)	22 (9.9)	19 (8.5)	
Good	82 (36.6)	23 (10.3)	11 (4.9)	26 (11.7)	22 (9.9)	
Fair	16 (7.1)	4 (1.8)	5 (2.2)	0 (0)	7 (3.1)	
Poor	2 (0.9)	0 (0)	1 (0.4)	0 (0)	1 (0.4)	
Self-report Physical Activity n (%)						
Sedentary	18 (8.0)	8 (3.6)	3 (1.3)	4 (1.8)	3 (1.3)	0.81
Mild	60 (26.8)	15 (6.7)	9 (4.0)	17 (7.6)	19 (8.5)	
Moderate	123 (54.9)	35 (15.7)	27 (12.1)	33 (14.8)	28 (12.6)	
Strenuous	22 (9.8)	7 (3.1)	5 (2.2)	5 (2.2)	5 (2.2)	
Smoking Status n (%)						
Current	19 (8.5)	6 (2.7)	1 (0.4)	8 (3.6)	4 (1.8)	0.37
Former	106 (47.3)	27 (12.1)	23 (10.3)	26 (11.6)	30 (13.4)	
Never	99 (44.2)	33 (14.7)	20 (8.9)	25 (11.2)	21 (9.4)	

$p$ -values for continuous measures are from tests for linear trend based on ANOVA, whereas  $p$ -values for categorical measures are based on  $\chi^2$  analysis.

**Table 2**—Adjusted\* mean (standard error) sleep characteristics by napping groups

Characteristic (N = 224)	0 N = 66	1 nap N = 44	2-3 naps N = 59	4 naps + N = 55	p-value for linear trend
Actigraphy nighttime sleep duration (h)	5.83 (0.10)	6.01 (0.12)	5.69 (0.11)	5.51 (0.11)	0.008 <sup>#</sup>
Actigraphy sleep efficiency (%) <sup>†</sup>	2.96 (0.04)	2.90 (0.05)	2.96 (0.05)	3.05 (0.05)	0.11
Untransformed (%)	81.70	82.83	81.70	79.88	
Actigraphy sleep latency (min) <sup>†</sup>	2.85 (0.09)	2.73 (0.11)	2.68 (0.09)	2.66 (0.10)	0.13
Untransformed (min)	16.29	14.33	13.59	13.30	
Epworth Sleepiness Scale	6.85 (0.48)	8.45 (0.59)	8.31 (0.51)	9.39 (0.52)	< 0.001
Pittsburgh Sleep Quality Index	6.47 (0.40)	6.42 (0.49)	6.40 (0.42)	6.52 (0.44)	0.95
Diary fatigue	0.69 (0.07)	0.67 (0.09)	0.85 (0.07)	0.98 (0.08)	0.002
Diary pain	0.53 (0.07)	0.36 (0.09)	0.44 (0.08)	0.76 (0.08)	0.03
Apnea-hypopnea Index <sup>†</sup>	2.33 (0.12)	2.04 (0.15)	2.29 (0.13)	2.16 (0.13)	0.64
Untransformed Index	9.28	6.69	8.87	7.67	

\*Analyses of covariance adjusted for age, race, gender, and depressive symptoms; <sup>#</sup>Significant race  $\times$  nap group interaction,  $p < 0.02$ ; <sup>†</sup>Variable is transformed; untransformed means provided for those variables without adjusting for age, race, gender, and depressive symptoms.

## DISCUSSION

Our study had three objectives. The first two objectives concerned whether participants who reported frequent daytime napping during the 10-day protocol had better or worse sleep over the nine nights, and within participants, whether napping during the day led to altered sleep the subsequent night or vice versa. Regarding the first objective, we found that African Americans who took more frequent naps averaged across nine nights had shorter nighttime sleep duration compared to Caucasians. Daytime sleepiness and fatigue were more frequently reported by frequent nappers. More frequent nappers also reported more bodily pain in their diaries. These findings were independent of age, gender, and depressive symptoms.

Regarding the second objective, our within-person analyses showed that taking a nap was associated with less efficient sleep measured by actigraphy the next night, and among African Americans only, taking a nap was associated with longer sleep latency the subsequent night. In addition, shorter nighttime sleep duration was associated with taking a longer nap the following day in all subjects. Goldman and colleagues<sup>11</sup> reported that taking longer naps was related to shorter sleep duration on the next night, and lower sleep efficiency was related to taking a longer nap the following day. Although the results from the two studies differ in the specific sleep measures involved, taken together, they suggest that short sleep duration and less efficient sleep can lead to napping and napping can lead to short and less efficient sleep. These findings offer empirical support for common behavioral treatment strategies in insomnia, namely, improving nighttime sleep consolidation and limiting daytime naps. Since napping led to poorer nighttime sleep efficiency, it follows that improving sleep efficiency (for instance, by restricting sleep opportunity) could reduce the need for naps. Conversely, reducing daytime naps could lead to improved sleep efficiency at night.

Our third objective was to identify whether persons who reported frequent napping had elevated cardiovascular risk factors. Our results showed that more frequent nappers had greater BMI and waist circumference, independent of age, race, gender, depressive symptoms, and AHI scores. These findings are consistent with the two studies showing that respondents who reported napping also reported being obese.<sup>8,26</sup> Thus, our findings provide the needed evidence that not only self-reported weight but measured weight and waist circumference are related to napping. While recent reviews of the evidence of relationships of sleep duration and obesity in adults have not been conclusive,<sup>27,28</sup> our findings of a relation-

ship between napping and weight argue that nap time should be considered when evaluating the relationship between sleep duration and obesity.

Our study has several limitations. First, the HeartSCORE study from which we recruited participants for SleepSCORE is a volunteer community sample interested in obtaining health information, and, therefore, may not be representative of the community at large. Second, we did not have information on the timing of the nap (e.g., morning, afternoon) in relation to nighttime sleep, so the impact of the *time of day of the nap* on subsequent sleep quality could not be determined. Third, the relationships identified in the nap group analyses cannot be considered causal due to the cross sectional nature of the study. However, the study has several strengths. The sample was multiethnic, with a sizeable number of African Americans. The duration of the protocol, 10 days and 9 nights of actigraphy and sleep diary data, makes our averaged sleep measures quite reliable. In addition, an objective measure of sleep disordered breathing was used in statistical analyses to control for its effects on the relationship of waist circumference and BMI, and napping behavior. Future studies should include more information on reasons for and timing of napping.

In summary, this study found that in middle-aged men and women, naps were associated with overall less nighttime sleep duration in African Americans and lower sleep efficiency as measured by actigraphy, and greater daytime sleepiness and fatigue. Taking a daytime nap was associated with lower sleep efficiency the following night, and shorter sleep duration at night was associated with taking a nap the following day. Frequent nappers show evidence of an increased risk for cardiovascular disease, through increased BMI and central adiposity. The effects of napping, and differences between racial/ethnic groups should be systematically examined in future studies examining sleep and health.

## ABBREVIATIONS

HeartSCORE, Heart Strategies Concentrating on Risk Evaluation  
 SleepSCORE, Sleep Strategies Concentrating on Risk Evaluation  
 PSG, polysomnography  
 AHI, apnea/hypopnea Index  
 PSQI, Pittsburgh Sleep Quality Index  
 ESS, Epworth Sleepiness Scale  
 BMI, body mass index

**Table 3**—Adjusted mean (standard error) biological characteristics by napping groups

Characteristic	0 N = 66	1 nap N = 44	2-3 naps N = 59	4 naps + N = 55	p-value for linear trend
Waist circumference (cm)	94.41 (1.61)	95.32 (2.00)	97.61 (1.71)	100.2 (1.77)	0.01
Body mass index (kg/m <sup>2</sup> )	28.79 (0.59)	29.22 (0.73)	29.44 (0.63)	31.46 (0.65)	0.004
Resting systolic blood pressure (mm Hg)	131.1 (1.81)	133.7 (2.24)	133.5 (1.92)	132.7 (1.98)	0.59
Resting diastolic blood pressure (mm Hg)	80.03 (1.25)	81.37 (1.55)	81.27 (1.33)	79.73 (1.37)	0.87

Analysis of covariance adjusted for age, race, gender, and depressive symptoms.

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## DISCLOSURE STATEMENT

This was not an industry support study. Dr. Buysse has consulted for Actelion, Arena, Cephalon, Eli Lilly, GlaxoSmithKline, Merck, Neurocrine, Neurogen, Pfizer, Respirationics, Sanofi-Aventis, Sepracor, Servier, Somnus Therapeutics, Stress Eraser, Takeda, and Transcept Pharmaceuticals, Inc. The other authors have indicated no financial conflicts of interest.