Short sleep duration is associated with decreased serum leptin, increased energy intake, and decreased diet quality in postmenopausal women

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Abstract

Objective—Short sleep duration induces hormonal perturbations contributing to hyperphagia, insulin resistance, and obesity. The majority of these studies are conducted in young adults. This analysis in a large (n= 769) sample of postmenopausal women (median age 63 y) sought to 1) confirm that sleep duration and sleep quality are negatively correlated with circulating leptin concentrations and 2) to examine the relationship between self-reported sleep, dietary energy intake, and diet quality, as well as, investigate the role of leptin in these associations.

Design and Methods—Sleep duration/quality, insomnia, and dietary intake were determined via self-report. Blood samples were collected following an overnight fast to assess serum leptin concentration. All analyses were adjusted for total body fat mass.

Results—Women reporting ≤6h sleep/night had lower serum leptin concentrations than those reporting ≥8h sleep (*P*= 0.04). Furthermore, those with ≤6h sleep/night reported higher dietary energy intake (p=0.01) and lower diet quality (P= 0.04) than the reference group (7h sleep/night).

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Conflicts of Interest

The authors declare that they have no competing interests.

Women sleeping   8h also reported lower diet quality than the reference group *(P*= 0.02). Importantly, serum leptin did not confound these associations.

Conclusions—These results provide evidence that sleep duration is inversely associated with serum leptin and dietary energy intake in postmenopausal women.

Keywords

obesity; sleep duration; sleep quality; leptin; energy intake; diet quality

Introduction

Overweight and obesity have reached epidemic proportions (1) and the prevalence of chronic sleep loss has corresponded with this rise in obesity (2). Evidence suggests that short sleep duration may be a risk factor for weight gain and obesity in adults and children (3–6) (3, 4).

Sleep deprivation experiments demonstrate that the energetic response to inadequate sleep is similar to the human metabolic adaptation to negative energy balance, resulting in increased phagic drive and weight gain. Animal (7–10) and human (11–14) studies support causal pathways linking short sleep duration with weight gain, obesity, and the development of diabetes. An increase in hunger, driven by a decrease in circulating leptin as shown in observational (11) and experimental (12–14) studies in humans supports this mechanism. These hormonal changes reduce the anorexigenic drive from leptin, which normally contributes to feelings of satiety and increases energy expenditure.

In light of the rising prevalence of obesity, the identification of interventions for the treatment and prevention of weight gain is a priority. Evidence shows that low quantity and quality of sleep may hinder the success of dietary interventions targeting obesity (15) and that women with better quality and habitual sleep of > 7h/night have greater long term weight loss (16). Moreover, sleep loss decreases resting energy expenditure and physical activity associated energy expenditure, as well as daily physical activity (15, 17, 18). Thus, further investigation of the metabolic and hormonal perturbations induced with sleep loss, as well as the resultant impact on dietary intake, is imperative.

Short sleep duration, sleep disturbance, and insomnia are highly prevalent in older women (19). Although the impact of sleep duration and quality on hormonal regulation of energy homeostasis is increasingly being investigated, the majority of these studies in humans, both epidemiological (5, 11) and experimental (12–14, 20, 21), have been conducted in young or middle aged individuals. Postmenopausal women have a high risk of weight gain and resultant metabolic pathophysiologies (22). Thus, understanding the relationship between sleep and dietary energy intake/diet quality is of particular importance in understanding such age-related weight gain and metabolic disease among postmenopausal women. The purpose of this study was to 1) evaluate the association between sleep duration/quality and circulating leptin concentrations in older women and 2) examine the role of leptin in the relationship between sleep, energy intake and diet quality.

Methods

Study Design and Participants

Participants from the Women's Health Initiative prospective Observational Study (WHI-OS) were recruited between 1994–1998 at 40 sites nationally. This analysis is restricted to women enrolled at the WHI Dual-energy X-ray Absorptiometry (DXA) centers (University of Arizona, University of Pittsburgh, and University of Alabama at Birmingham). The WHI-OS was designed to investigate risk factors for women's health, including osteoporosis, cancer and cardiovascular diseases and has been previously described (23). Leptin, sleep, diet, DEXA, and anthropometric data were collected at baseline (n= 1001; 878 with complete dietary data) and studied cross-sectionally for these analyses. Because both sleep disturbance and disordered eating is frequent in individuals diagnosed with depression (24), 109 women were excluded for depression based on the Center for Epidemiologic Studies Depression Scale (CES-D short form cutoff of >0.06) (25), leaving a final sample of 769 women. This study was reviewed and approved by the Human Subjects Review Committee at each participating institution.

Covariates

Self-administered or interviewer-administered questionnaires for eligibility screening and baseline characteristics (such as demographic, reproductive, and health status data) were completed by each of the WHI-OS participants at baseline. At time of enrollment, physical examinations, including weight and height measurements, were conducted by trained WHI staff.

Dietary energy intake and diet quality

Dietary energy intake was assessed at enrollment via the self-administered WHI Food Frequency Questionnaire, which reports consumption frequency and portion size over the previous 3 months. Because it has been previously described that self-reported energy intake was underreported in the WHI participant population (26), we utilized a mathematical calibration model to quantify daily dietary energy intake formulated from doubly-labeled water studies in a sub-sample of WHI participants (27). Diet Quality was estimated using the Alternate Healthy Eating Index (AHEI-2005) score (28). The AHEI was designed to assess diet quality based on foods and nutrients predictive of chronic disease risk and was created by summing its 9 component scores (fruit, vegetable, ratio of white to red meat, trans fat, ratio of polyunsaturated to saturated fat, total fiber, nuts and soy, alcohol consumption, and long-term multivitamin use) with each of the nine components having a potential score of 0–10 and a total AHEI score of 0–90, with a higher score corresponding to higher diet quality.

Subjective measures of sleep duration and quality

At enrollment, participants were asked the following sleep-related questions estimating behavior over the prior 4 weeks: 1) Did you have trouble falling asleep? 2) Did you wake up several times at night? 3) Did you wake up earlier than you planned to? 4) Did you have trouble getting back to sleep after you woke up too early? 5) Did you snore? 6) Overall, how was your typical night's sleep during the past 4 weeks? 7) About how many hours of sleep

did you get on a typical night during the past 4 weeks? Questions 6 and 7 were used to asses sleep quality and quantity, respectively. Sleep duration variables included the following categories: (1) 5h or less, (2) 6h, (3) 7h, (4) 8h, (5) 9h, and (6) 10h or more. For data analysis, categories 1 and 2 were collapsed to create 6h and categories 4–6 were collapsed to create 8h. Questions 1–5, comprising the 5-item Women's Health Initiative validated Insomnia Rating Scale (WHIIRS) (29), assessed sleep latency, sleep maintenance insomnia, early morning awakening, and sleep quality. For each question, the score ranged from 0–4; summary scores range from 0–20, with a higher score indicating insomnia.

Body Composition

Total body fat and lean mass was determined via DXA as previously described (30).

Plasma Leptin Concentrations

Blood specimens were collected from each participant after a 12-h overnight fast at baseline and within the four weeks that the sleep-related questions referred to. Blood was processed within 1h of collection and aliquoted plasma was stored at −80°C. Total serum leptin concentrations were assayed using a bead-based, suspension multiplex assay on a Luminex 100 analyzer and the data were interpreted using software developed at Rules-Based Medicine (Human Multi-Analyte Profile (MAP) version 1.6, Rules Based Medicine, Austin, TX, USA). For each multiplex, both calibrators and controls were included on each microtiter plate. Testing results were determined first for the high, medium and low controls for each multiplex to ensure proper assay performance.

Statistical Analysis

Medians (interquartile ranges) and numbers (%) were used to describe baseline characteristics of subjects. Dietary energy and leptin values were natural log transformed prior to analysis of covariance (ANCOVA) and regression analysis. Physical activity (total MET hours per week) was square-root transformed. A comorbidity variable was created from women who answered positively to having hypertension, rheumatoid arthritis, or diabetes at baseline. The association of untransformed leptin values by sleep duration and sleep quality categories was explored using Kruskal Wallis tests. Comparison of leptin values by sleep duration and sleep quality categories were performed using ANCOVA, adjusting for age, race/ethnicity, smoking status, and total body fat mass. Multiple linear regression analysis was used to determine the association between dietary energy, diet quality, and percent kilocalories (kcal) from carbohydrate, protein, and fat with sleep predictors. Previous studies have reported an association with chronic disease risk with a cut-point of 7h/sleep per night, therefore a reference group of 7h sleep/night was used here in the multiple linear regression analyses. Models were built using a phased approach, including predictors which were identified 'a priori', and were significantly associated with dietary energy and/or diet quality in the sample population. Final models were adjusted for age (y), race/ethnicity (non-Hispanic white, Hispanic/Latino), total body fat mass (kg), physical activity (MET h/week), income (< $20,000, $20,000–34,999, $35,000–49,999, $50,000), education (< College or College or Above), smoking status (never user, past user, current user), alcohol intake (non-drinker, past drinker, <1 drink/month, < 1 drink/week, 1 to < 7 drinks/week, 7+drinks/week), comorbidity (yes/no) and leptin (ng/ml). P-values were 2-

tailed and statistical significance was set at <0.05. Statistical analyses were performed using STATA 12 (STATA, College Station, TX) and SAS 9.3 (SAS Institute, Cary, NC).

Results

Participant Characteristics

The characteristics of participants are summarized in Table 1. Most participants were non-Hispanic whites; with a median age of 63 years; 41% had a normal BMI. Median daily calibrated dietary energy intake was 2021 kcal, while the median AHEI value was 41.2. 33.7% of participants reported sleeping 6h/night. Forty nine percent reported having very sound or restful/sound or restful sleep.

Leptin and Sleep Quality and Sleep Duration

It is well established that serum leptin concentrations are highly correlated with fat mass (31, 32) as was shown here (R^2= 0.494, P<0.0001). Thus, we utilized total body fat mass as a covariate when comparing leptin concentrations, dietary energy, and diet quality by sleep duration and sleep quality categories. ANCOVA analyses of categorized sleep duration and sleep quality adjusted for age, race, total body fat mass, and smoking status revealed that log leptin values differed significantly over sleep duration categories. Specifically, participants reporting 6h sleep demonstrated lower circulating leptin concentrations than those reporting 8h sleep (*P*= 0.04) (Figure 2A). Leptin concentrations were not different between sleep quality categories (Figure 2B).

Association of Calibrated Dietary Energy Intake with Sleep

To investigate the relationship between sleep and dietary energy intake/quality and to determine if leptin served as a mediator of these associations, we performed multiple linear regression analyses using models including, and not including leptin. Results of these analyses are summarized in Table 2. Daily dietary energy intake was associated with sleep duration when controlling for the covariates listed in model 2, independent of leptin. Women who reported sleeping 6h/night demonstrated a 1% increase in mean dietary energy intake relative to women who reported sleeping 7h/night (reference group) (*P*=0.01) (Table 2). Women reporting "very restless/restless" sleep had higher daily energy intake intercepts (P= 0.03). However, this association was not significant after controlling for covariates listed in model 2 and leptin concentrations (Table 2).

Association of Diet Quality with Sleep Predictors

Diet quality was significantly associated with sleep duration and this association remained after addition of leptin to the model (Table 2). Women who reported sleeping 8h *(P*= 0.02) had significantly lower diet quality intercepts than women who slept for 7h. This inverse relationship was also significant among women who reported sleeping 6h (*P*=0.04). Women reporting the lowest category of sleep quality ("very restless or restless") had lower diet quality intercepts than women reporting very sound or restful/sound or restful sleep (*P*= 0.04), independent of leptin concentrations (Table 2). To further explore the relationship between diet quality and sleep, we investigated the association of sleep predictors with macronutrient intake. While sleep duration was not significantly associated with the

composition of macronutrient intake, we found that women who reported average quality sleep consumed a lower percent of kcal from carbohydrate than women who reported sound/very sound sleep in both the crude (P=0.011) and age, ethnicity, and total body fat mass adjusted models (P=0.015). Women who reported restless/very restless sleep consumed a higher percentage of kcal from fat than women who reported sound/very sound sleep in crude models (P=0.016). However, these associations were no longer statistically significant on adjustment for covariates in models 2 and 3. The WHI insomnia scale was not significantly associated with diet quality, dietary energy intake, or the macronutrient composition of dietary energy intake.

Discussion

To our knowledge, this study is the first to examine the association of sleep duration and quality with leptin in the context of dietary energy intake and diet quality among post-menopausal women. Our study shows significantly higher energy intake among women sleeping 6h/night. Although apparently modest, based on the average energy intake of the participants in this study, this 1% increase in daily energy intake in the form of fat could result in excess of an estimated 7373 kcal/year, equivalent to 0.8 kg of extra body lipid. Our finding that short sleep duration is associated with decreased serum leptin, is consistent with results from some, but not all, epidemiological studies of sleep duration and likely supports the role of many other physiological mediators of leptin. Some of these studies have been conducted in obese populations, in which, leptin insensitivity separates serum leptin from leptin signaling. Circadian rhythm can also affect serum leptin. Finally, when examining the effect of leptin one must segregate effects of adiposity from those of leptin. The altered leptin signaling and regulation in the obese, the circadian changes in leptin, and the statistical correction for adiposity may explain why some studies have not shown an association between sleep and leptin, dietary energy, and diet quality.

It has been reported that in hyperleptinemic obese people short sleep duration is not associated with a decrease in leptin (33, 34). Knutson et al. (34) found that leptin controlled for fat mass was not associated with objectively measured (actigraphy) sleep duration or quality in a cohort of 80 obese men and premenopausal obese women (mean BMI of 37.5 and 38.4 in men and women, respectively) aged 18–50 years (34). Similarly, an intervention study conducted by Littman et al. in 173 postmenopausal, inactive women (aged 50–75 y, mean BMI 30.5) reported that neither subjectively reported sleep duration or sleep quality was associated with serum leptin at baseline (35). In contrast, Taheri et al. reported that in a study of men and women with a mean age of 52.7 and median BMI of 29.7 (26.2, 34.7 IQR), objectively (polysomnography) and subjectively (sleep log) measured short sleep duration was, in fact, associated with reduced leptin, independent of BMI and sex (11). The participants in the study of Knutson et al. have BMI values close to morbid obesity (BMI 40), while the participants in the studies of Littman et al. and Taheri et al. have BMI values representing the lower end of obesity. Thus, the degree of obesity may impact leptin values in relation to lifestyle factors such as sleep.

Differences in the measure of sleep, methods of sleep quality assessment, markers of adiposity and statistical analyses may also contribute to the differences in reported results. In

our study, sleep duration and quality was measured by subjective sleep logs and questionnaires versus objective measurements of polysomnography and actigraphy as measured by Hayes et al. (33) and Knutson et al. (34), respectively. We utilized total body fat mass as a covariate when analyzing the association of sleep variables with leptin while Knutson et al. calculated a relative leptin level by dividing leptin by body fat percentage. However, the studies of Littman et al. and Taheri et al. utilized BMI as a covariate rather than fat mass. Leptin is secreted from adipocytes in proportion to body fat stores and is, thus, tightly correlated with fat mass (31, 32). Because physiological factors associated with increased adiposity, such as respiratory disorders (i.e. sleep apnea) can impact sleep duration and quality, it is imperative to control for fat mass when examining the association between sleep and leptin.

Circulating leptin concentrations have a discrete circadian rhythm with levels rising to maximum at night and dropping to minimum during the day (36, 37). To limit changes associated with the diurnal cycle, our study and the aforementioned studies (11, 35) (34) collected blood samples at one time point after an overnight fast. Variations in bed-time and waking time may, however, confound the relationship between sleep duration and leptin. Previous studies have investigated the impact of sleep curtailment on the diurnal rhythm of circulating leptin (13, 21) and these studies provide detail of the disruptive impact of sleep duration on the diurnal rhythm of leptin release, causing a reduction in the amplitude of the diurnal variation of circulating leptin concentrations. Because we do not have data on bed time or waking time on the day of blood sampling in our study population, we cannot confirm that blood sampling took place within a specific window of this circadian rhythm for all subjects. Another potential limitation of this study is the time frame described in the FFQ compared to that of the sleep-related questions. The FFQ queried about food type and quantity over the previous 3 months and the sleep-related questions were in the context of the previous 4 weeks. However, the participants completed these 2 questionnaires at the same time and did so within 4 weeks of blood collection.

While the association between sleep duration, energy intake, energy expenditure, and hormones that regulate intake and expenditure has been described (7–10), there are sparse data describing the association between sleep and diet quality. This study demonstrates that diet quality is significantly associated with sleep duration and that this relationship is independent of serum leptin concentration. It is interesting to note the "U" shaped relationship between sleep duration and diet quality among the participants of our study. That is, women sleeping ≥8h had significantly lower diet quality than women who slept for 7h, while women sleeping ≤6 hours also demonstrated lower diet quality than the 7h reference group. Given the previously discussed hormonal changes that stimulate hyperphagic drive, some studies have investigated the relationship between short sleep duration and eating habits, most of which conclude that short sleep duration is associated with increased intake of calories from snacks and carbohydrates (38, 39), eating behaviors that could reduce the overall diet quality score. Our findings that percent kcal from carbohydrate and fat were significantly associated with self-reported sleep quality suggests that sleep quality may also be associated with macronutrient diet composition supporting lower overall diet quality. These associations, however, were attenuated on adjustment for covariates known to modulate macronutrient intake. What is less clear is why sleeping >8h

per night is associated with decreased diet quality in this study. Future studies examining the impact of sleep duration on diet quality in postmenopausal women would be worthwhile to elucidate these findings.

Given the previously discussed hormonal changes that stimulate hyperphagic drive, some studies have investigated the relationship between short sleep duration and eating habits. It has been recently reported that neuronal activity among healthy men and women aged 35 to 45 y in response to food stimuli is enhanced after experimentally restricted sleep compared to habitual sleep, providing evidence that sleep curtailment influences brain centers that affect food choices (40). Similarly, a study in young females (18–28 y) described an inverse relationship between sleep duration and diet quality (38). To our knowledge, our study is the first to examine this relationship in a large population of older, postmenopausal women. Our observation that post-menopausal women with better sleep quality had higher values of diet quality suggests that both sleep duration and sleep quality may have an impact on food cravings and food choices. Although causal relationships cannot be determined by this cross-sectional analysis, it is possible that differences in food intake among our study population are impacting sleep habits. However, data from previously discussed experimental studies of induced sleep restriction suggest that sleep affects dietary energy intake and diet quality under controlled conditions.

We have demonstrated that sleep duration, but not sleep quality is associated with fat mass-adjusted circulating leptin in a large sample of post-menopausal women. Additionally, we have described an inverse relationship between sleep duration and dietary energy intake, as well as sleep duration/quality and diet quality. These findings suggest that sleep may be a relevant factor in weight management. While suggestive that 7h sleep per night and improved sleep quality could help augment other approaches to improve dietary choices in postmenopausal women, a clinical trial would be needed to test such hypotheses. Given the increased risk of metabolic disorders and obesity with menopause, our findings provide evidence that improving sleep duration and quality may be a novel target for a lifestyle intervention aimed at modulating dietary energy intake and diet quality in post-menopausal women.

Acknowledgments

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What is already known about this subject?

- Observational and experimental studies in humans have shown that short sleep duration induces a decrease in circulating leptin, an increase in hunger ratings, and an increase in adiposity.

- Evidence also shows that low quantity and quality of sleep may hinder the success of dietary interventions targeting obesity.

- The majority of these studies have been conducted in young adults.

What does this study add?

- This analysis demonstrates that postmenopausal women reporting ≤6h sleep/night had lower fat-mass-adjusted serum leptin concentrations than those reporting ≥8h sleep, while women reporting 7h sleep/night did not differ from those sleeping ≤6h or ≥8h sleep/night.

- Linear regression analyses using 7h sleep per night as a reference group shows that postmenopausal women reporting ≤6h sleep/night reported significantly higher dietary energy intake and lower diet quality than those with 7h/night. These associations were independent of circulating leptin concentrations.
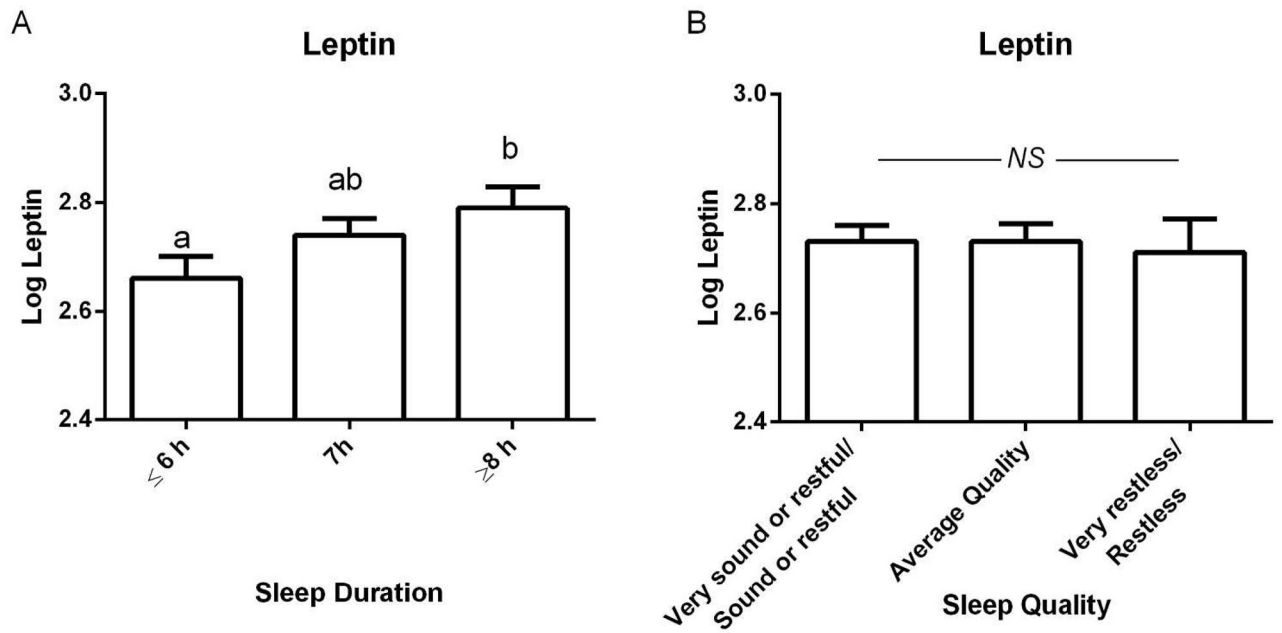
Figure 1.
Circulating leptin concentrations partitioned by A) sleep duration and B) sleep quality. Values presented as least square mean ± SEM, adjusted for age, race, fat mass, and smoking status; superscripts that differ indicate differences between sleep duration categories, ANCOVA bonferroni corrected $P<0.05$.

Table 1

Characteristics of Study Participants

Variable	Median	IQR[1]
Leptin (ng/ml)	16	(10,27)
Calibrated energy intake (kcal/d)	2021.0	(1908,2134.3)
Alternate Healthy Eating Index (AHEI) at baseline	41.2	(33.3,48.9)
WHI Insomnia Rating Scale	5.0	(3,9)
Age at screening (years)	63.0	(57,69)
Total body fat mass (kg)	28.0	(22,35.2)
Physical activity (Total METS/week)	9.8	(3.7,19.9)
Weight (kg)	67.2	(59.4,76.5)
Body Mass Index (kg/m^2)	25.9	(23.1,29.4)
	No	%
Sleep Duration		
<=6 hours	256	33.7
7 hours	299	39.3
>=8 hours	205	27.0
Sleep Quality		
Very sound or restful/Sound or restful	374	49.1
Average quality	297	39.0
Very restless/restless	91	11.9
Ethnicity		
White non-Hispanic	561	73.0
Hispanic/Latino	208	27.0
Smoking Status		
Never smoked	425	56.1
Past smoker	282	37.2
Current smoker	51	6.7
Alcohol Intake		
Non-drinker	91	11.9
Past drinker	134	17.5
< 1 drink per month	95	12.4
< 1 drink per week	170	22.2
1 to < 7 drinks per week	202	26.3
7+ drinks per week	75	9.8
HRT Usage Status		
Never used	352	45.8
Past user	102	13.3
Current user	315	41.0
Hypertension Ever (Baseline)		
No	553	72.8

Variable	Median	IQR[1]
Yes	207	27.2
Diabetes at Screening		
No	726	94.4
Yes	43	5.6
Arthritis Ever (Baseline)		
No	386	51.1
Yes	369	48.9
Rheumatoid Arthritis		
No arthritis	386	51.1
Rheumatoid arthritis	37	4.9
Other/Missing	332	44.0
Comorbidity Status		
No diabetes/hypertension/rheumatoid arthritis	522	67.9
Hypertension/diabetes/rheumatoid arthritis	247	32.1
Income		
< $20,000	209	27.2
$20,000–34,999	209	27.2
$35,000–49,999	141	18.3
>= $50,000	210	27.3
Education		
< College	508	66.5
College or Above	256	33.5
Body Mass Index Category		
Underweight (<18.5 kg/m^2)	11	1.4
Normal weight (18.5–24.9 kg/m^2)	318	41.4
Overweight (25–29.9 kg/m^2)	271	35.2
Obese (>= 30 kg/m^2)	169	22.0

[1]IQR = Interquartile Range (25th, 75th percentiles)

Table 2

The association between sleep duration, sleep quality and WHI Insomnia Scale with dietary energy intake and diet quality score.

	ln* Dietary Energy Intake (kcal/day)			Diet Quality (AHEI)		
	Coeff	SE	p	Coeff	SE	p
Sleep Duration						
Crude						
<= 6 hours	0.008	0.008	0.338	−2.755	0.943	**0.004**
7 hours	Ref	-	-	Ref	-	-
>= 8 hours	0.007	0.008	0.384	−2.375	1.031	**0.022**
Adjusted Model 1[a]						
<= 6 hours	0.007	0.004	0.129	−2.246	0.905	**0.013**
7 hours	Ref	-	-	Ref	-	-
>= 8 hours	0.0001	0.004	0.975	−2.341	0.987	**0.018**
Adjusted Model 2[b]						
<= 6 hours	0.009	0.004	**0.015**	−1.511	0.784	0.054
7 hours	Ref	-	-	Ref	-	-
>= 8 hours	0.001	0.004	0.808	−2.168	0.873	**0.013**
Adjusted Model 3[c]						
<= 6 hours	0.009	0.004	**0.014**	−1.634	0.779	**0.036**
7 hours	Ref	-	-	Ref	-	-
>= 8 hours	0.001	0.004	0.814	−2.077	0.872	**0.017**
Sleep Quality						
Crude						
Very Sound or Restful/Sound or Restful	Ref	-	-	Ref	-	-
Average Quality	0.005	0.007	0.510	−1.148	0.883	0.194
Very restless/Restless	0.025	0.012	**0.033**	−4.346	1.180	**0.000**
Adjusted Model 1[a]						
Very Sound or Restful/Sound or Restful	Ref	-	-	Ref	-	-
Average Quality	0.002	0.004	0.641	−1.117	0.853	0.191

	ln* Dietary Energy Intake (kcal/day)			Diet Quality (AHEI)		
	Coeff	SE	p	Coeff	SE	p
Very restless/Restless	0.005	0.006	0.376	−3.384	1.154	**0.004**
Adjusted Model 2[b]						
Very Sound or Restful/Sound or Restful	Ref	-	-	Ref	-	-
Average Quality	0.004	0.004	0.259	−0.969	0.750	0.197
Very restless/Restless	0.003	0.005	0.503	−2.204	1.080	**0.042**
Adjusted Model 3[c]						
Very Sound or Restful/Sound or Restful	Ref	-	-	Ref	-	-
Average Quality	0.004	0.004	0.259	−0.979	0.748	0.191
Very restless/Restless	0.003	0.005	0.504	−2.241	1.069	**0.036**
WHI Insomnia Scale						
Crude	−0.0001	0.0009	0.893	−0.1361	0.0903	0.132
Adjusted Model 1[a]	−0.0001	0.0004	0.715	−0.1020	0.0902	0.258
Adjusted Model 2[b]	<−0.0001	0.0004	0.933	−0.0530	0.0808	0.512
Adjusted Model 3[c]	<−0.0001	0.0004	0.933	−0.0534	0.0806	0.508

ln, natural log

[a] Adjusted for age, race/ethnicity and total body fat mass

[b] Adjusted for the variables in Model 1 plus sqrt(physical activity), income, education, smoking status, alcohol intake, antidepressant use and comorbidity status (diabetes/hypertension/rheumatoid arthritis)

[c] Adjusted for the variables in Model 2 plus circulating ln leptin concentrations