Role of Sleep Duration and Quality in the Risk and Severity of Type 2 Diabetes Mellitus

Kristen L. Knutson, PhD; Armand M. Ryden, MD; Bryce A. Mander, BA; Eve Van Cauter, PhD

Background: Evidence from laboratory and epidemiologic studies suggests that decreased sleep duration or quality may increase diabetes risk. We examined whether short or poor sleep is associated with glycemic control in African Americans with type 2 diabetes mellitus.

Methods: We conducted a cross-sectional study of volunteers with type 2 diabetes interviewed at the University of Chicago Hospitals, Chicago, Ill. The final analysis included 161 participants. Glycemic control was assessed by hemoglobin A_{1c} (HbA_{1c}) level obtained from medical charts. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI). Perceived sleep debt was calculated as the difference between preferred and actual weekday sleep duration.

Results: The mean ± SD sleep duration was 6.0 ± 1.6 hours, and 71% of the participants were classified as having poor quality sleep (PSQI score >5). We excluded patients with sleep frequently disrupted by pain (n = 39). In patients without diabetic complications, glycemic control was associated with perceived sleep debt but not PSQI score. The predicted increase in HbA_{1c} level for a perceived sleep debt of 3 hours per night was 1.1% above the median. In patients with at least 1 complication, HbA_{1c} level was associated with PSQI score but not perceived sleep debt. The predicted increase in HbA_{1c} level for a 5-point increase in PSQI was 1.9% above the median.

Conclusions: In our sample, sleep duration and quality were significant predictors of HbA_{1c}, a key marker of glycemic control. Combined with existing evidence linking sleep loss to increased diabetes risk, these data suggest that optimizing sleep duration and quality should be tested as an intervention to improve glucose control in patients with type 2 diabetes.

Arch Intern Med. 2006;166:1768-1774

CHRONIC PARTIAL SLEEP LOSS due to bedtime restriction and sleep complaints are increasingly prevalent in modern society. During the past few years, evidence from laboratory and epidemiologic studies has accumulated, suggesting that decreased sleep duration and/or quality may adversely effect glucose regulation and increase the risk of type 2 diabetes mellitus.

Two published laboratory studies have reported alterations in glucose regulation during partial sleep restriction. In the first study, exposure to 5 days of 4-hour sleep durations was associated with a 40% reduction in glucose tolerance to intravenous glucose and a 30% reduction in the acute insulin response to glucose.[1] These findings were confirmed in another study that used a randomized cross-over design with 2 nights of sleep restriction or extension (4-hour vs 10-hour bedtimes).[2] After the second night of each condition, caloric intake was replaced by constant intravenous glucose infusion, and blood samples were collected every 20 minutes. After sleep restriction, morning glucose levels were higher and insulin levels were lower than after sleep extension.[2] Preliminary data from an ongoing study revealed a marked reduction in glucose tolerance and insulin sensitivity after 8 nights of 5-hour bedtimes compared with 8-hour bedtimes.[3] The consistency of these findings, despite differences in experimental design, suggests that sleep restriction has adverse effects on glucose metabolism.

A much larger number of epidemiologic studies, summarized in **Table 1**, have explored the relationship between sleep duration and/or quality and diabetes. The prospective studies, which involved different geographical locations, were remarkably consistent, indicating that short or poor sleep may increase the risk of developing type 2 diabetes. Evidence from cross-sectional studies suggests that a diabetic condition may involve a reduction in sleep duration or an impairment of sleep quality. Neuropathic pain and nocturia have been suggested as 2 possible causes of decreased sleep quality.[14]

Author Affiliations: Department of Medicine, University of Chicago (Drs Knutson, Ryden, and Van Cauter, and Mr Mander); and Institute for Neuroscience, Northwestern University (Mr Mander); Chicago, Ill.

Table 1. Summary of Epidemiologic Studies That Examined the Association Between Sleep and Diabetes

Source	Study Design	Sample	Results
Ayas et al[4]	Prospective (10-y follow-up)	Nurses Health Study, married female nurses aged 30-55 y in 1976	Increased risk of incident diabetes associated with sleep durations of 6 h or less relative to 7-8 h (RR for ≤5 h, 1.29; 95% CI, 1.05-1.58; RR for 6 h, 1.16; 95% CI, 1.02-1.32); however, association is lost when adjusting for BMI (RR for ≤5 h, 1.18; 95% CI, 0.96-1.44; RR for 6 h, 1.10; 95% CI, 0.97-1.25).
Kawakami et al[5]	Prospective (8-y follow-up)	2649 Japanese men, begun in 1984	Incident diabetes was associated with high frequency of difficulty initiating sleep (HR, 2.98; 95% CI, 1.36-6.53) or difficulty maintaining sleep (HR, 2.23; 95% CI, 1.08-4.61).
Nilsson et al[6]	Prospective (7- to 22-y follow-up)	Swedish men, 35-51 y in 1974-1984	Increased risk of incident diabetes among men who reported difficulty falling asleep or use of sleeping pills (OR for reporting either, 1.52; 95% CI, 1.05-2.20).
Mallon et al[7]	Prospective (12-y follow-up)	1187 Swedish men and women	Increased risk of incident diabetes among men who reported difficulty maintaining sleep (RR, 4.8; 95% CI, 1.9-12.5) or who reported sleep duration of 5 h or less (RR, 2.8; 95% CI, 1.1-7.3). No significant associations between sleep and diabetes risk was observed among women.
Bjorkelund et al[8]	Prospective (32-y follow-up)	600 Swedish women, begun in 1968-1969	No association between the incidence of diabetes and the self-reported sleep problems, sleep medication use, or sleep duration at baseline.
Meisinger et al[9]	Prospective (average, 7.5-y follow-up)	8269 Nondiabetic German men and women aged 25-74 y at baseline	Significant increased risk of incident type 2 diabetes for those who reported difficulty maintaining sleep at baseline (HR from most adjusted model for men, 1.60; 95% CI, 1.05-2.45; HR for women, 1.98; 95% CI, 1.20-3.29).
Yaggi et al[10]	Prospective (15- to 17-y follow-up)	Massachusetts Male Aging Study, 1709 men aged 40-70 y in 1987-1989	Sleep duration ≤6 h/night was associated with twice the risk of developing diabetes (RR for ≤5 h, 1.95 [95% CI, 0.95-4.01]; RR for 6 h, 1.95 [95% CI 1.06-3.58]) relative to 7 h.
Gislason and Almqvist[11]	Cross-sectional	3000 Swedish men in 1984-1985	A higher proportion of men with diabetes mellitus reported difficulty maintaining sleep (21.9% vs 7.5%), difficulty initiating sleep (21.1% vs 6.9%), and excessive daytime sleepiness (12.2% vs 5.8%) relative to all men combined.
Hyyppa and Kronholm[12]	Cross-sectional	877 Diabetic patients and nondiabetic controls, aged 45-64 y from Finland	No difference in mean bedtime, awakening time, total sleep time, naps, and nocturnal sleep between the diabetic patients and controls.
Sridhar and Madhu[13]	Cross-sectional	184 Patients with diabetes and 99 controls from India	Difficulty maintaining sleep (12% vs 7%), difficulty initiating sleep (21% vs 0%), and excessive daytime sleepiness (1.1% vs 0.8%) were more common in the diabetic patients.
Lamond et al[14]	Cross-sectional	74 Patients with diabetes from Australia	Severity of type 2 diabetes, assessed by questionnaire, was associated with longer sleep onset ($r = 0.29$; $P<.05$) and increased sleep fragmentation ($r = 0.24$; $P<.05$), and this relationship appeared primarily mediated by nocturia and pain.

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; OR, odds ratio; RR, risk ratio.

While there is extensive laboratory and epidemiologic evidence for an adverse effect of sleep-related breathing disorder (SRBD) on insulin sensitivity and risk for the metabolic syndrome,[15-21] there is less published data on the incidence of SRBD in patients with type 2 diabetes. One study from Sweden had indicated that the prevalence of severe obstructive sleep apnea in men with type 2 diabetes is 36%, more than double that found in normoglycemic subjects.[22]

The rapidly accumulating evidence for a relationship between impaired sleep and diabetes risk raises the possibility that an association between reduced sleep duration or quality and the severity of an existing diabetic condition may exist. We therefore present the results of a study that examined self-reported sleep duration and quality and glycemic control as assessed by hemoglobin A_{1c} (HbA_{1c}) levels in African Americans with type 2 diabetes.

METHODS

The study involved a 30- to 45-minute interview and access to medical charts. The protocol was approved by the University of Chicago institutional review board, and all participants gave written informed consent. The participants received $20 for participating. Patients with type 2 diabetes were recruited at the University of Chicago Hospital, Chicago, Ill. A total of 298 patients (216 African Americans, 54 whites, 3 Hispanics, 1 Asian, and 24 of other or undetermined ethnicity) completed the study. The sample composition was consistent with the ethnic distribution of the local patient population.

Our study planned to exclude patients from the analysis who were diagnosed as having type 2 diabetes within the past year because it is unlikely that they had achieved stable glycemic control (n=24). Patients who provided incomplete responses to the sleep questionnaire (n=7), patients without a glycated hemoglobin (GHb) or HbA_{1c} measurement within 3 months of the interview (n=38), patients claiming to prefer 12 or more hours of sleep per night (n=7), and patients of unknown ethnicity (n=18) were also excluded. The final sample included 204 individuals (161 African Americans, 38 whites, and 5 of other ethnicities). There are well-documented ethnic differences in both diabetes risk and sleep.[23,24] In an exploratory analysis, the interaction between our measure of sleep quality and race was a highly significant predictor of glycemic control ($P<.001$), indicating that the analysis needed to be stratified by race. Ethnic groups other than African Americans are, however, underrepresented in our sample. The present analysis therefore focuses only on African American patients.

During the interview, waist-hip ratio was measured, and the patients reported height and weight from which we calculated body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared). The questions on diabetes and its complications were part of the University of Chicago Diabetes/Quality of Life survey study,[25] and thus this information was all self-reported. Frequency of checking glucose level, diabetes medications, and frequency of exercise were assessed. Subjects were categorized as either taking insulin (alone or in combination with oral antidiabetic agents) or not taking insulin. The presence of major complications of diabetes (neuropathy, retinopathy, nephropathy, coronary artery disease, and peripheral vascular disease) was also assessed. This variable was dichotomized into absence of complications and presence of 1 or more complications.

The interview included the Pittsburgh Sleep Quality Index (PSQI),[26] a validated 19-item questionnaire that produces a global sleep quality score that ranges from 0 to 21, derived from 7 component scores.[27,28] A global score greater than 5 distinguishes poor sleepers from good sleepers.[26] The question "how often have you had trouble sleeping because you had pain?" identified patients with sleep disturbed by pain as those who responded "3 or more times per week." We excluded these individuals in our analyses of the association between sleep and glycemic control because chronic pain is a likely confounder. The PSQI also included the actual number of hours of sleep obtained on weekdays and on weekends. A weekly average was calculated using the following formula:

(5/7 × Weekday Sleep Duration) + (2/7 × Weekend Sleep Duration).

We also asked preferred sleep duration and calculated perceived sleep debt as the difference between weekday sleep duration and preferred sleep duration. We created a modified PSQI score by removing the sleep duration component to assess sleep quality independently from sleep quantity.

The PSQI does not assess the presence of SRBD, which is frequent in type 2 diabetes.[22] However, the PSQI includes questions about breathing and snoring, which we used to estimate risk of SRBD. Subjects were classified as at high risk of SRBD if they indicated on the PSQI that their sleep was disturbed 3 or more times per week because of difficulty breathing or coughing or snoring. Subjects who responded that their bed partners had noticed loud snoring or pauses in breathing during sleep 1 or more times per week were also classified as at high risk. Finally, this high-risk group included 12 patients who indicated during the interview that they had SRBD. All other subjects were classified as at low risk of SRBD.

The interview included the 20-item Center for Epidemiologic Studies Depression Scale (CES-D).[29] Scores range from 0 to 60, where a higher score indicates greater depressive symptoms.

We obtained total GHb or HbA_{1c} values from the medical charts. Midway through the study, the University of Chicago Laboratories switched from measuring GHb (by Bio-Rad Variant Classic boronate affinity-automated high-performance liquid chromatography [HPLC]) to HbA_{1c} (by Bio-Rad Variant II ion exchange automated HPLC) (Bio-Rad Laboratories, Hercules, Calif). The intra-assay coefficient of variation was 0.5% to 1.0%, and the interassay coefficient of variation was 2.2% to 2.4% for both methods. We converted GHb values to HbA_{1c} using the following equation:

$HbA_{1c} = 0.72 \times GHb + 1.35$.[30]

All statistical analyses were computed using SPSS 13.0 (SPSS Inc, Chicago, Ill). Hemoglobin A_{1c} had a right-skewed distribution. Therefore, we used the natural log of HbA_{1c} ($lnHbA_{1c}$) in correlation and general linear model (GLM) analysis. Perceived sleep debt was used as the primary variable to quantify the impact of sleep duration because it incorporates individual differences in sleep need. We also repeated the analyses using weekly sleep duration rather than perceived sleep debt. We used the modified PSQI score as a marker of sleep quality. Finally, we calculated GLM for the dependent variable, $lnHbA_{1c}$, including both categorical and continuous variables. The first model included 2 sleep variables as well as covariates and all first-degree interactions. Interactions with a P level of $>.05$ were removed one at a time by deleting the interaction with the largest P value. Because a significant interaction term that includes a sleep variable and a categorical variable indicates that the association between sleep and glycemic control is different for the different categories, we planned to stratify our regression analyses according to any significant interactions that included a categorical variable and a sleep variable.

RESULTS

The sample included 42 men and 119 women. **Table 2** provides descriptive statistics. The mean HbA_{1c} level was 8.3%, and 26% of the sample had an HbA_{1c} level below 7%, which is the recommended optimal upper level of HbA_{1c}.[31] Only 6% of patients reported obtaining at least 8 hours of sleep on weeknights and only 22% obtained at least 7 hours. Approximately 71% of the patients exceeded the cutoff for poor sleep (ie, global PSQI score >5). We separated the 39 patients who reported sleep frequently disrupted by pain from the remainder of the sample. Sleep quantity was lower in the group with pain, indicated by shorter sleep durations and greater perceived sleep debt (Table 2). Modified PSQI scores were also higher in the group with frequent pain, even after excluding the pain question from the score.

The proportion of patients with poor sleep quality (global PSQI score >5) remained high (67%) after subjects with pain-disturbed sleep were excluded. The remainder of our analysis was restricted to patients without pain-disturbed sleep (35 men and 87 women). The only significant sex difference in sleep was for weekend sleep duration, which was significantly longer in women (6.6 ± 1.8 hours vs 5.9 ± 1.3 hours; $P = .03$).

In bivariate analyses, higher $lnHbA_{1c}$ levels were associated with higher scores on the modified PSQI ($r = 0.28$; $P = .002$), ie, lower sleep quality, a greater perceived sleep debt ($r = 0.30$; $P = .001$), and shorter weekly sleep durations ($r = -0.17$; $P = .03$). Higher depression scores were also associated with higher $lnHbA_{1c}$ levels ($r = 0.27$; $P = .003$). As expected, the depression score and the modified PSQI score were significantly correlated ($r = 0.63$; $P < .001$). Body mass index, waist-hip ratio, frequency of exercise, frequency of checking glucose, and duration of diabetes were not significantly related to $lnHbA_{1c}$ levels. Finally, younger participants had poorer glycemic control ($r = -0.27$; $P = .002$).

We performed a GLM analysis of variance, with $lnHbA_{1c}$ level as the dependent variable and perceived sleep debt, modified PSQI score, age, sex, BMI, insulin use, presence of diabetic complications, and 6 first-degree interactions as predictors. After controlling for age, sex, BMI, diabetic complications, and insulin use, the sleep variables were significant (perceived sleep debt, $P = .01$; modified PSQI score, $P = .04$) and had significant interactions with diabetic complications (diabetic

complications × modified PSQI score, $P=.001$) and insulin use (insulin use × perceived sleep debt, $P=.03$; insulin use × modified PSQI score, $P=.02$). Adding the CES-D depression score as a predictor only marginally increased the variance accounted for by the model (from unadjusted $r^2=0.40$ to $r^2=0.41$). The depression score did not emerge as a significant predictor or have significant interactions with other predictors. Replacing perceived sleep debt with weekly sleep duration revealed a significant main effect of sleep duration ($P=.02$) and a trend for modified PSQI score ($P=.06$), and the interactions between the sleep variables and the presence of complications or the use of insulin remained significant. Because of the significant interactions between the sleep variables and diabetic complications or insulin use, regression analyses were stratified by diabetic complications and by insulin use (**Table 3**).

In patients without complications, perceived sleep debt but not subjective sleep quality was associated with $\ln HbA_{1c}$ levels. In contrast, in patients with at least 1 complication, modified PSQI score, but not perceived sleep debt, was a significant predictor after controlling for covariates. **Figure 1** presents bivariate associations between HbA_{1c} level and the 2 sleep variables in patients without and with diabetic complications.

Since we used $\ln HbA_{1c}$ in regression analyses, the β coefficients of the GLM represent the proportional change in HbA_{1c} level for an absolute change in main effect.[32] **Figure 2** presents the predicted increase in HbA_{1c} level for hypothetical patients with low (ie, corresponding to the 25th percentile of HbA_{1c} values), average (ie, corresponding to the 50th percentile of HbA_{1c} values), and high (ie, corresponding to the 75th percentile of HbA_{1c} values) HbA_{1c} levels. For example, in patients without complications, a perceived sleep debt increase of 3 hours per night for an individual with an HbA_{1c} level of 7.5% predicts an HbA_{1c} level of 8.6% (ie, an increase by 1.1%). In patients with at least 1 complication, a 5-point increase in PSQI for an individual with an HbA_{1c} of 8.7% predicts an HbA_{1c} level of 10.6% (ie, an increase by 1.9%). Because the β coefficient is proportional, changes in sleep variables have a larger effect at larger values of HbA_{1c}.

Table 3 also presents results for patients stratified by insulin use. For patients not taking insulin, perceived sleep debt, but not PSQI, was a significant predictor. For patients taking insulin, PSQI score, but not perceived debt, was significantly associated with $\ln HbA_{1c}$ level.

Of the 122 patients, 23 (19%) were classified as at high risk of SRBD. This subgroup had a higher mean HbA_{1c} level compared with those at low risk of SRBD (9.7 vs 7.9%; $P<.01$) but were not more likely to have complications or to be treated with insulin. The bivariate correlations between HbA_{1c} level and sleep variables were essentially unchanged after excluding subjects at high risk of SRBD ($\ln HbA_{1c}$ level and perceived sleep debt, $r=0.30$ [$P=.003$]; $\ln HbA_{1c}$ level and modified PSQI, $r=0.23$ [$P<.05$]).

Table 2. Characteristics of Patients*

Characteristic	Full Sample (n = 161)	No Frequent Pain (n = 122)	Frequent Pain (n = 39)
Age, y	57.3 ± 12.5	58.3 ± 12.7	54.3 ± 11.5
HbA_{1c}, %	8.3 ± 2.1	8.2 ± 2.1	8.5 ± 2.2
BMI	35.8 ± 9.8	35.3 ± 9.7	37.4 ± 10.4
Waist-hip ratio	0.95 ± 0.11	0.95 ± 0.12	0.96 ± 0.10
Hours of sleep on weekdays	6.0 ± 1.6	6.2 ± 1.6	5.2 ± 1.7†
Hours of sleep on weekends	6.1 ± 1.7	6.4 ± 1.6	5.4 ± 1.8†
Weekly sleep duration average	6.0 ± 1.6	6.3 ± 1.5	5.3 ± 1.6†
Preferred hours of sleep	7.7 ± 1.3	7.8 ± 1.3	7.5 ± 1.3†
Perceived sleep debt, h/night	1.8 ± 1.5	1.7 ± 1.5	2.4 ± 1.5†
Modified PSQI score (no sleep duration component)	7.0 ± 3.8	6.0 ± 3.2	10.0 ± 4.0†
CES-D score	15.2 ± 10.9	12.8 ± 9.2	22.5 ± 12.5†
Years of diabetes	11.4 ± 9.3	11.5 ± 9.3	11.1 ± 9.5
Diabetic complications, No.†			
0	52.8	57.4	38.5
≥1	47.2	42.6	61.5
Insulin use†			
No insulin	50.3	56.7	34.2
Insulin	47.8	43.3	65.8
Frequency checking glucose†			
Never	5.0	5.7	2.6
1-2/wk	8.1	6.6	12.8
3-6/wk	6.8	7.4	5.1
1/d	23.6	27.9	10.3
2/d	34.1	35.2	30.8
3/d	15.5	13.1	23.1
≥4/d	6.8	4.1	15.4
Frequency of exercise per wk			
Rarely	32.2	28.7	43.6
1	11.2	13.9	2.6
2	16.8	17.2	15.4
3	13.0	13.1	12.8
≥4	26.7	27.0	25.6

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CES-D, Center for Epidemiologic Studies Depression Scale; HbA_{1c}, hemoglobin A_{1c}; PSQI, Pittsburgh Sleep Quality Index.

*Data are given as mean ± SD or percentage unless otherwise indicated.

†Indicates a significant difference in means or proportions between the no frequent pain and frequent pain groups according to *t* tests or χ^2 tests ($P<.05$).

COMMENT

Recent laboratory and epidemiologic studies have indicated that insufficient sleep may result in decreased glucose tolerance and increased diabetes risk.[1,4,6,9,33] The findings also raise the possibility that reduced sleep duration or quality could adversely affect glucose control in an existing diabetic condition. To our knowledge, the present study is the first to address this hypothesis by examining self-reported sleep duration and quality and HbA_{1c} levels in patients with type 2 diabetes. Our analyses reveal that a higher perceived sleep debt or lower sleep quality are associated with poorer glucose control, after controlling for age, sex, BMI, insulin use, and the presence of major complications.

Table 3. Predictors of $lnHbA_{1c}$ From GLM Regression Analysis Stratified by Diabetic Complications and Insulin Use*

	Diabetic Complications, No.		Insulin Use	
Main Effects	**0**	**≥1**	**No Insulin Use**	**Using Insulin**
Age	−0.005 (.03)	−0.002 (.52)	0.001 (.74)	−0.007 (.004)
Sex (male reference group)	−0.023 (.70)	−0.100 (.21)	−0.069 (.29)	−0.025 (.69)
BMI	−0.001 (.60)	0.004 (.29)	0.002 (.47)	−0.001 (.62)
Perceived sleep debt	0.51 (.04)	−0.005 (.85)	0.061 (.01)	−0.017 (.51)
Modified PSQI score	−0.014 (.16)	0.043 (.002)	−0.009 (.44)	0.026 (.02)
Insulin use	0.083 (.12)	0.115 (.09)	NA	NA
Diabetic complications	NA	NA	0.031 (.59)	0.074 (.22)
Adjusted r^2	0.12	0.22	0.05	0.30

Abbreviations: BMI, body mass index; GLM, general linear model; $lnHbA_{1c}$, natural log of hemoglobin A_{1c}; NA, not applicable; PSQI, Pittsburgh Sleep Quality Index.

*Data are given as β coefficient (*P* value) unless otherwise specified.

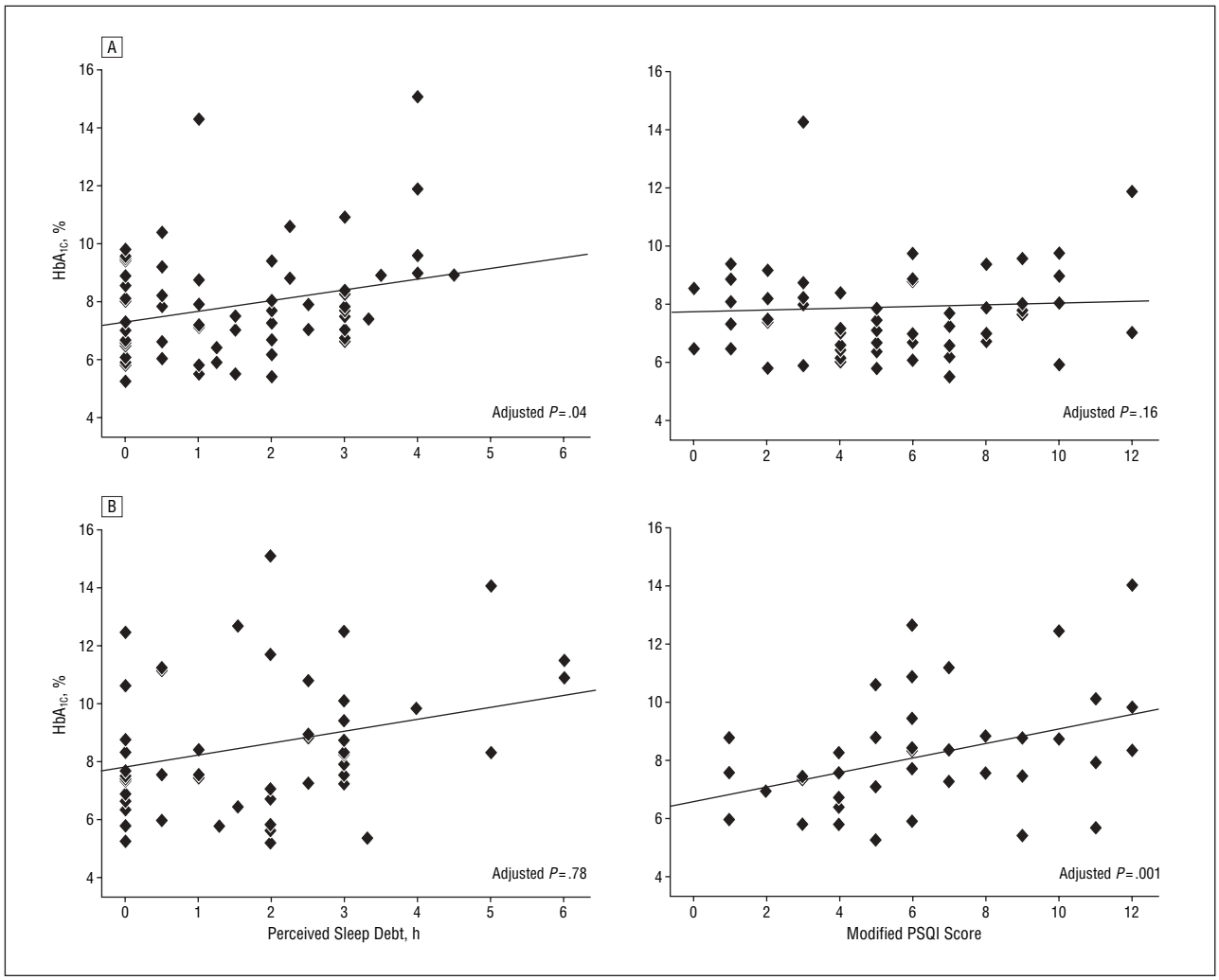

Figure 1. Scatterplots between hemoglobin A_{1c} (HbA_{1c}) and modified Pittsburgh Sleep Quality Index (PSQI) score and perceived sleep debt stratified by diabetic complications (A, no diabetic complications; B, ≥1 diabetic complications). Note the interindividual variability of HbA_{1c} levels at any given level of modified PSQI score or perceived sleep debt value.

The direction of causality cannot be inferred from our analyses. Poor glycemic control in patients with diabetes could impair subjective sleep quality even in the absence of pain. For example, nocturia could play a role in the observed relationship between sleep and glycemic control.[14] One of the limitations of our study is that the questionnaires did not include assessment of the severity of nocturia. Perceived sleep debt could partly reflect the inability to achieve sufficient sleep rather than a voluntary reduction of bedtime. The fact that most patients

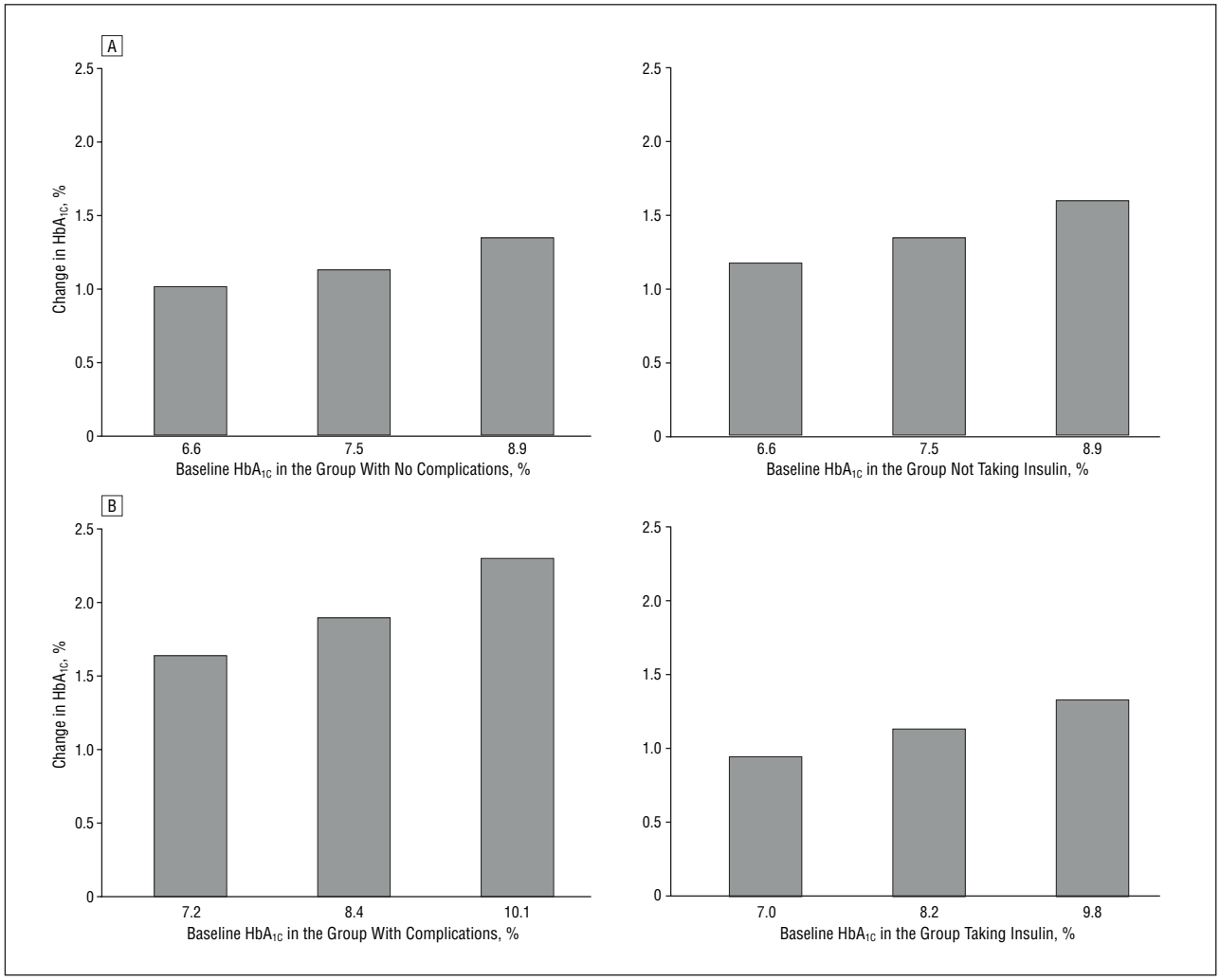

Figure 2. Predicted increase in hemoglobin A_{1c} (HbA_{1c}) resulting from an increase in perceived sleep debt (A) or a decrease in sleep quality (ie, an increase in Pittsburgh Sleep Quality Index [PSQI] score) (B) in a hypothetical subject who would have a baseline HbA_{1c} in the low (25th percentile), median (50th percentile), or high (75th percentile) for the subgroup under consideration. The predicted change is based on an increase in perceived sleep debt of 3 hours for the group with no complications and the group not taking insulin. The predicted change is based on an increase in PSQI score by 5 points for the group with complications and the group taking insulin.

(83%) without pain-disrupted sleep did not report longer sleep during the weekend relative to weekdays is consistent with this notion. Thus, poor diabetes control could contribute both to a higher perceived sleep debt and lower sleep quality. On the other hand, evidence from previous laboratory and epidemiologic studies supports the opposite direction of causality, that is, that short or poor sleep impairs glucose control. The prospective studies showing a relationship between sleep duration and the development of symptomatic diabetes are particularly relevant to the present findings. Intervention studies are needed to test the hypothesis that paying a sleep debt and/or improving sleep quality may improve glucose control in patients with type 2 diabetes. The strength of the associations in our sample suggests that such studies would be warranted from a clinical standpoint. Our analyses indicated that in patients without complications, a perceived sleep debt of 3 hours per day was associated with an increase in HbA_{1c} level by 1.1% above the median, while in patients with at least 1 complication, a 5-point increase in PSQI score (decreased sleep quality) was associated with an increase in HbA_{1c} level by 1.9% above the median. The magnitude of these effects is comparable to those of widely used oral antidiabetic agents.[34-36] The fact that perceived sleep debt is significant for those without complications or those not taking insulin, while sleep quality, as measured by the modified PSQI, is significant for those with complications or those taking insulin, may be due to differences in severity of disease.

The present study introduces the construct of "perceived sleep debt" that captures habitual sleep time and subjective sleep need. In exploratory bivariate analyses, we noted that perceived sleep debt was more strongly correlated with levels of HbA_{1c} compared with sleep duration ($r=+0.30$ vs $r=-0.17$), which suggested that perceived sleep debt may be a better predictor of glycemic control because it represents sleep loss in relation to subjective sleep need, which likely varies between individuals. We verified that the results of the regression model would have been qualitatively similar had we used sleep duration rather than perceived sleep debt but noted that

perceived sleep debt accounted for a larger proportion of the variance compared with sleep duration.

Approximately 20% of our participants (17% of men and 27% of women) were identified as at high risk for SRBD. Others have found a 36% prevalence of SRBD in men with type 2 diabetes,[22] while the prevalence in the general population has been estimated to be 24% in men and 9% in women.[37] Our method of identifying SRBD using questions from the PSQI has not been validated, and it is possible that we have underestimated the prevalence of SRBD in this sample. When patients classified as being at high risk for SRBD were excluded from our analysis, the associations between HbA_{1c} levels and sleep variables persisted, indicating that SRBD risk as estimated in our study is not the primary mediator of the relationship between glucose control and sleep.

The present study identifies sleep as a potential factor influencing glucose control in a specific population of patients with type 2 diabetes. African Americans represent approximately 18% of the 19 million Americans with type 2 diabetes.[38] Similar associations between sleep and glucose control are likely to exist in other ethnic groups. A cohort study that included mostly whites found a relationship between sleep duration and the development of symptomatic diabetes.[4] Additional research is needed to determine whether optimizing sleep duration and quality may improve glucose control in patients with type 2 diabetes. Sleep curtailment has become increasingly prevalent in modern society, and it cannot be excluded that this behavior has contributed to the current epidemic of type 2 diabetes.

Accepted for Publication: June 23, 2006.
Correspondence: Eve Van Cauter, PhD, Department of Medicine, University of Chicago, 5841 S Maryland Ave, MC1027 AMB M239, Chicago, IL 60637 (evcauter@medicine.bsd.uchicago.edu).
Author Contributions: The senior author had full access to the study data and takes responsibility for its integrity and the accuracy of the analysis.
Financial Disclosure: None reported.
Funding/Support: This work was supported by grants from the MacArthur Foundation, Chicago, Ill; the American Diabetes Association, Alexandria, Va; and the National Institutes of Health (RO1 DK-41814 and PO1 AG-11412), Bethesda, Md.
Role of the Sponsors: The sole role of the sponsors was financial support.

REFERENCES

1. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet*. 1999;354:1435-1439.
2. Spiegel K, Knutson K, Leproult R, Tasali E, Cauter EV. Sleep loss: a novel risk factor for insulin resistance and type 2 diabetes. *J Appl Physiol*. 2005; 99:2008-2019.
3. Leproult R, Holmback U, Van Cauter E. Marked decrease in insulin sensitivity following one week of partial sleep deprivation with or without circadian misalignment. *Diabetes*. 2006;55(suppl 1):A323-A324.
4. Ayas NT, White DP, Al-Delaimy WK, et al. A prospective study of self-reported sleep duration and incident diabetes in women. *Diabetes Care*. 2003;26:380-384.
5. Kawakami N, Takatsuka N, Shimizu H. Sleep disturbance and onset of type 2 diabetes. *Diabetes Care*. 2004;27:282-283.
6. Nilsson PM, Roost M, Engstrom G, Hedblad B, Berglunc G. Incidence of diabetes in middle-aged men is related to sleep disturbances. *Diabetes Care*. 2004; 27:2464-2469.
7. Mallon L, Broman JE, Hetta J. High incidence of diabetes in men with sleep complaints or short sleep duration: a 12-year follow-up study of a middle-aged population. *Diabetes Care*. 2005;28:2762-2767.
8. Bjorkelund C, Bondyr-Carlsson D, Lapidus L, et al. Sleep disturbances in midlife unrelated to 32-year diabetes incidence: the prospective population study of women in Gothenburg. *Diabetes Care*. 2005;28:2739-2744.
9. Meisinger C, Heier M, Loewel H. Sleep disturbance as a predictor of type 2 diabetes mellitus in men and women from the general population. *Diabetologia*. 2005; 48:235-241.
10. Yaggi HK, Araujo AB, McKinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. *Diabetes Care*. 2006;29:657-661.
11. Gislason T, Almqvist M. Somatic diseases and sleep complaints: an epidemiological study of 3,201 Swedish men. *Acta Med Scand*. 1987;221:475-481.
12. Hyyppa MT, Kronholm E. Quality of sleep and chronic illnesses. *J Clin Epidemiol*. 1989;42:633-638.
13. Sridhar GR, Madhu K. Prevalence of sleep disturbances in diabetes mellitus. *Diabetes Res Clin Pract*. 1994;23:183-186.
14. Lamond N, Tiggemann M, Dawson D. Factors predicting sleep disruption in type II diabetes. *Sleep*. 2000;23:415-416.
15. Ip MS, Lam B, Ng MM, Lam WK, Tsang KW, Lam KS. Obstructive sleep apnea is independently associated with insulin resistance. *Am J Respir Crit Care Med*. 2002; 165:670-676.
16. Punjabi NM, Shahar E, Redline S, Gottlieb DJ, Givelber R, Resnick HE. Sleep-disordered breathing, glucose intolerance, and insulin resistance: the Sleep Heart Health Study. *Am J Epidemiol*. 2004;160:521-530.
17. Punjabi NM, Sorkin JD, Katzel LI, Goldberg AP, Schwartz AR, Smith PL. Sleep-disordered breathing and insulin resistance in middle-aged and overweight men. *Am J Respir Crit Care Med*. 2002;165:677-682.
18. Vgontzas AN, Papanicolaou DA, Bixler EO, et al. Sleep apnea and daytime sleepiness and fatigue: relation to visceral obesity, insulin resistance, and hypercytokinemia. *J Clin Endocrinol Metab*. 2000;85:1151-1158.
19. Coughlin SR, Mawdsley L, Mugarza JA, Calverley PM, Wilding JP. Obstructive sleep apnoea is independently associated with an increased prevalence of metabolic syndrome. *Eur Heart J*. 2004;25:735-741.
20. Svatikova A, Wolk R, Gami AS, Pohanka M, Somers VK. Interactions between obstructive sleep apnea and the metabolic syndrome. *Curr Diab Rep*. 2005; 5:53-58.
21. Tassone F, Lanfranco F, Gianotti L, et al. Obstructive sleep apnoea syndrome impairs insulin sensitivity independently of anthropometric variables. *Clin Endocrinol (Oxf)*. 2003;59:374-379.
22. Elmasry A, Lindberg E, Berne C, et al. Sleep-disordered breathing and glucose metabolism in hypertensive men: a population-based study. *J Intern Med*. 2001; 249:153-161.
23. Disdier-Flores OM, Rodriguez-Lugo LA, Perez-Perdomo R, Perez-Cardona CM. The public health burden of diabetes: a comprehensive review. *P R Health Sci J*. 2001;20:123-130.
24. Durrence HH, Lichstein KL. The sleep of African Americans: a comparative review. *Behav Sleep Med*. 2006;4:29-44.
25. Meltzer D, Egleston B. How patients with diabetes perceive their risk for major complications. *Eff Clin Pract*. 2000;3:7-15.
26. Buysse DJ, Reynolds CF III, Monk TH, Berman SB, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28:193-213.
27. Buysse DJ, Monk TH, Reynolds CF, Mesiano D, Houck PR, Kupfer DJ. Patterns of sleep episodes in young and elderly adults during a 36-hour constant routine. *Sleep*. 1993;16:632-637.
28. Carpenter JS, Andrykowski MA. Psychometric evaluation of the Pittsburgh Sleep Quality Index. *J Psychosom Res*. 1998;45:5-13.
29. Radloff L. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1:385-401.
30. Toney LJ, McLawhon RW, Zibrat SJ. Evaluation and comparison of hemoglobin HbA1c on the Bio-Rad Variant II to total glycated hemoglobin on the Bio-Rad Variant Hemoglobin Testing Systems [abstract]. *Clin Chem*. 2001;47:A4.
31. American Diabetes Association. Standards of medical care in diabetes—2006. *Diabetes Care*. 2006;29(suppl 1):S4-42.
32. Gujarati D. *Basic Econometrics*. 3rd ed. New York, NY: McGraw-Hill, Inc; 1995.
33. Gottlieb DJ, Punjabi NM, Newman AB, et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. *Arch Intern Med*. 2005;165:863-868.
34. Duckworth W, Marcelli M, Padden M, et al. Improvements in glycemic control in type 2 diabetes patients switched from sulfonylurea coadministered with metformin to glyburide-metformin tablets. *J Manag Care Pharm*. 2003;9:256-262.
35. Garber AJ, Donovan DS Jr, Dandona P, Bruce S, Park JS. Efficacy of glyburide/metformin tablets compared with initial monotherapy in type 2 diabetes. *J Clin Endocrinol Metab*. 2003;88:3598-3604.
36. Moses R. Repaglinide in combination therapy. *Diabetes Nutr Metab*. 2002;15:33-38.
37. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med*. 1993; 328:1230-1235.
38. Mokdad AH, Ford ES, Bowman BA, et al. Diabetes trends in the US: 1990-1998. *Diabetes Care*. 2000;23:1278-1283.