High Incidence of Diabetes in Men With Sleep Complaints or Short Sleep Duration

A 12-year follow-up study of a middle-aged population

LENA MALLON, MD, PHD[1]
JAN-ERIK BROMAN, PHD[1]
JERKER HETTA, MD, PHD[2]

OBJECTIVE — The aim of this study was to investigate the possible relationship among sleep complaints, sleep duration, and the development of diabetes prospectively over a 12-year period in a middle-aged Swedish population.

RESEARCH DESIGN AND METHODS — A random sample of 2,663 subjects aged 45–65 years living in mid-Sweden were sent a postal questionnaire including questions about sleep complaints, sleep duration, sociodemographic characteristics, behavioral risk factors, medical conditions, and depression (response rate 70.2%). Twelve years later, a new questionnaire with almost identical questions was sent to all the survivors (n = 1,604) in 1995, and the questionnaire was answered by 1,244 subjects (77.6%).

RESULTS — Men reporting new diabetes at follow-up more often reported short sleep duration (≤5 h per night) (16.0 vs. 5.9%, $P < 0.01$), difficulties initiating sleep (16.0 vs. 3.1%, $P < 0.001$), and difficulties maintaining sleep (28.0 vs. 6.3%, $P < 0.001$) at baseline than men who did not develop diabetes. Women reporting new diabetes at follow-up reported long sleep duration (≥9 h per night) more often at baseline than women not developing diabetes (7.9 vs. 2.4%, $P < 0.05$). In multiple logistic regression models, the relative risk (95% CI) for development of diabetes was higher in men with short sleep duration (2.8 [1.1–7.3]) or difficulties maintaining sleep (4.8 [1.9–12.5]) after adjustment for age and other relevant risk factors. Short or long sleep duration or sleep complaints did not influence the risk of new diabetes in women.

CONCLUSIONS — Difficulties maintaining sleep or short sleep duration (≤5 h) are associated with an increased incidence of diabetes in men.

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Diabetes is associated with increased frequency of sleep complaints (1–4), and this may be due to the disease itself as well as to physical complications of the disease (3,5). However, sleep disturbances may also play a primary role in the pathophysiology of diabetes. Data have demonstrated that individuals suffering from poor sleep have increased arousal and increased physiological activation (6–13). Experimentally induced sleep debt has been found to be associated with increased activation in the hypothalamic-pituitary-adrenal axis as indexed by elevated evening cortisol levels and impaired glucose tolerance (14). These findings indicate that disturbance and curtailment of sleep may be risk factors for the development of insulin resistance. The insulin resistance syndrome, also known as the metabolic syndrome, is a cluster of risk factors for adult-onset diabetes, and it usually consists of obesity, dyslipidemia, hyperglycemia, and hypertension (15).

In a sample of healthy middle-aged men in Sweden, Nilsson et al. (16) found that difficulties in falling asleep or regular use of hypnotic drugs was associated with development of diabetes when adjustment was made for several risk factors. A 10-year follow-up survey of women aged 30–55 years enrolled in the Nurses Health Study in the U.S. has shown that both short and long sleep increased the risk of symptomatic diabetes after multivariate adjustment for standard risk factors (17). In an 8-year prospective study of male employees of an electrical company in Japan, Kawakami et al. (18) reported a high incidence of diabetes in male subjects reporting "difficulties initiating sleep often or almost every day" or "difficulties maintaining sleep often or almost every day", after controlling for other factors relevant to type 2 diabetes.

An important risk factor that should be ruled out or controlled in studies investigating the association among sleep complaints, deviant sleep duration, and diabetes is depression. Sleep complaints and altered sleep patterns are diagnostic criteria for depression (19), and studies have also shown that depression increases the risk of diabetes (20–22).

The aim of this study was to investigate the possible relationship among sleep complaints, deviant sleep duration, and the development of diabetes prospectively over a 12-year period in a middle-aged Swedish population, controlling for potential risk factors including depression.

RESEARCH DESIGN AND METHODS

— The aim with the original cohort in 1983 was to estimate the prevalence of sleep complaints and certain mental and physical complaints in relation to insomnia and use of hypnotic medication in a middle-aged population. From the population register, 2,663 men and women aged 45–65 years were randomly selected from the County of Dalarna in central Sweden, constituting 4% of the population in the county at the time, and 1,870 (70.2%) questionnaires were completely filled in. The responders were representative of the entire popula-

From the [1]Department of Neuroscience, Psychiatry, University Hospital, Uppsala, Sweden; and the [2]Karolinska Institutet, Neurotec/Psychiatry, Karolinska University Hospital, Huddinge, Sweden.

Address correspondence and reprint requests to Lena Mallon, MD, PhD, Department of Neuroscience, Psychiatry, University Hospital, SE-751 85 Uppsala, Sweden. E-mail: lena.mallon@ltdalarna.se.

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Abbreviations: BNSQ, Basic Nordic Sleep Questionnaire; SSI, Sleep Sufficiency Index; USI, Uppsala Sleep Inventory.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

tion at the time of the study regarding age and sex (23). A new questionnaire was sent to all the survivors (n = 1,604) in 1995, and the questionnaire was, after one reminder, answered by 1,244 subjects (77.6%).

Questionnaires

Both questionnaires have been described in detail before (24,25). The questionnaire used in 1983 consisted of 80 questions concerning demographic and lifestyle variables, medical conditions, depression, snoring, and sleeping difficulties. The questionnaire used in 1995 consisted of 84 questions, and a majority of questions were identical to those used in 1983.

In both surveys, marital status was defined as married or not married (i.e., single, divorced, widowed, or separated), living conditions were defined as living alone or with someone else, and smoking was defined as currently smoking or not. Alcohol habits were categorized into nonuse and use of alcohol. Questions were asked about body weight and height, and BMI (weight in kilograms divided by the square of height in meters) was calculated. Diabetes and hypertension were ascertained by asking subjects (in two yes or no questions) whether they had diabetes or hypertension. Depression was assessed by the question "Do you feel depressed?" to be answered by yes or no.

In both surveys, there were questions adopted from the Uppsala Sleep Inventory (USI), which has previously been used in epidemiological studies (26). The questions focus on the severity of sleep complaints, and they do not specify any time frame. Subjects were asked about difficulties initiating sleep and difficulties maintaining sleep, and the questions were to be answered on a 5-point scale (1 = no problems, 2 = minor problems, 3 = moderate problems, 4 = severe problems, and 5 = very severe problems). At least severe problems (scores 4 and 5) were considered to be a complaint, and this cutoff was used in the analysis. Regarding time frame, the Basic Nordic Sleep Questionnaire (BNSQ) (27) was added in the 1995 questionnaire. The BNSQ focuses on the frequency of sleep complaints during the last 3 months on a 5-point scale (1 = never or less than once a month, 2 = less than once a week, 3 = once or twice a week, 4 = three to five times a week, and 5 = daily or almost daily). In 1995, 86.3% of subjects reporting scores 4 or 5 (at least severe complaints of difficulties initiating sleep) on the USI reported scores of 4 or 5 for the BNSQ question about difficulties initiating sleep (at least complaints three to five times a week during the last 3 months). Regarding difficulties maintaining sleep, 94.0% of subjects reporting scores 4 or 5 on the USI reported scores of 4 or 5 in the BNSQ question about difficulties maintaining sleep. Thus, the majority of subjects reporting severe difficulties initiating sleep or difficulties maintaining sleep (USI) have had this problem for at least 3 months.

In the question about snoring, subjects were asked to state the frequency of "loud and disturbing snoring" on a 5-point scale. The five alternatives in the answer were never, seldom, occasionally, often, and very often. Subjects reporting snoring loud and disturbing often or very often (scores 4 and 5) were considered as habitual snorers. Duration of sleep was assessed by asking subjects to estimate habitual night sleep time, and the answer was expressed as a continuous variable. Subjects were also asked to estimate habitual sleep need, and the Sleep Sufficiency Index (SSI), the ratio of amount of estimated habitual sleep time to the amount of estimated need for sleep expressed as a percentage), was calculated.

The study was approved by the Ethics Committee of the Faculty of Medicine at Uppsala University in Sweden.

Nonresponders

Of subjects who were alive at follow-up, 360 did not answer the questionnaire. There was no sex difference in nonresponse. The nonresponders were older, more often living alone, not married, and smoking. Female nonresponders reported difficulties initiating sleep more often than responders: 12.9 vs. 7.3% (χ^2 = 7.2; $P < 0.01$). There was no difference in reported sleep time or in prevalence of medical conditions reported at baseline.

Statistics

Statistical analysis was performed on a Macintosh computer, using the statistical analysis program SPSS 10.0 (SPSS, Chicago, IL). Standard methods were used to calculate mean values and SDs. The χ^2 test was used for comparison between categorical variables, and when the comparison involved continuous variables, the t test was used. The influence of multiple variables was analyzed using multiple logistic regression analysis. The results are presented as adjusted relative risks (RRs) with 95% CIs. The minimum statistical significance level for all analyses was $P < 0.05$. Separate analyses were developed for men and women to explore potential sex differences in the nature of associations, and estimates were adjusted for age in 5-year strata.

RESULTS — Of the 1,244 subjects who responded to the questionnaires in 1983 and 1995, 1,187 (95.4%) answered the question about diabetes in both surveys, and the following analyses are based on those subjects. In 1983, 17 (1.4%) reported diabetes. Of the 1,170 without diabetes in 1983, 88 reported diabetes (new diabetes) in 1995 whereas 1,082 continued not to have diabetes.

The incidence of diabetes in our population was 7.5% (6.1% in women and 9.1% in men). The incidence was 30.4% in men with difficulties maintaining sleep and 21.0% in men with sleep duration of ≤5 h. Both women and men reporting new diabetes were older and more often obese (BMI ≥30 kg/m^2) at baseline, but they lost weight during the follow-up period in comparison with subjects not developing diabetes (Table 1).

In our sample there was no sex difference in reports of sleep time (7.0 ± 1.1 h), but women reported a need for longer sleep time (7.5 ± 1.0 vs. 7.3 ± 0.8 h, t = 3.0, $P < 0.01$). The SSI showed no sex difference (95.1 ± 12% for men and 94.1 ± 13% for women).

Men with new diabetes had a shorter sleep time and lower SSI than men who did not develop diabetes. Women with new diabetes reported long sleep duration (≥9 h per night) more often, and they were less often smokers at baseline compared with women without new diabetes. Men reporting new diabetes at follow-up were more often living alone. They reported snoring, short sleep duration (≤5 h per night), difficulties initiating sleep, and difficulties maintaining sleep more often at baseline compared with men not developing new diabetes.

Tables 2 and 3 summarize the results from logistic regression analyses to determine the independent factors at baseline influencing the risk of new diabetes during the 12-year follow-up for women and men. After adjustment for age, obesity was associated with significantly increased risk of incident diabetes in women. Living alone, obesity, snoring, depression, short sleep duration (≤5 h per night), and having difficulties initiating sleep and difficulties maintaining

Table 1—*Baseline characteristics and risk factors in 1983 for incident diabetes in men and women*

Reported variable or symptom in 1983	Women			Men		
	New diabetes	No diabetes	*P* value	New diabetes	No diabetes	*P* value
n	38	582		50	500	
Age (years)	56.8 ± 5.3	54.6 ± 6.0	0.034	56.0 ± 5.8	54.2 ± 5.9	0.039
BMI (kg)	28.7 ± 4.3	25.1 ± 3.6	<0.001	28.7 ± 3.6	25.1 ± 2.6	<0.001
ΔBMI (kg)	−1.0 ± 3.4	0.9 ± 3.0	0.001	−0.6 ± 2.1	0.4 ± 1.7	<0.001
Sleep time (h)	6.8 ± 1.2	7.0 ± 1.1	NS	6.6 ± 1.3	7.0 ± 1.1	0.025
Sleep need (h)	7.4 ± 1.1	7.5 ± 1.0	NS	7.4 ± 0.9	7.3 ± 0.8	NS
SSI (%)	92.4 ± 14.1	94.2 ± 12.9	NS	90.1 ± 16.0	95.6 ± 11.6	0.002
Not married	9 (23.7)	113 (19.4)	NS	2 (4.0)	35 (7.0)	NS
Living alone	5 (13.2)	63 (10.8)	NS	11 (22.0)	44 (8.8)	0.002
Hypertension	8 (21.1)	101 (17.4)	NS	4 (8.0)	70 (14.0)	NS
Obesity (BMI ≥30 kg/m^2)	15 (39.5)	51 (8.8)	<0.001	13 (26.0)	19 (3.8)	<0.001
Smoking	2 (5.3)	109 (18.7)	0.038	9 (18.0)	103 (20.6)	NS
Alcohol use	10 (26.3)	214 (36.8)	NS	50 (58.0)	309 (61.8)	NS
Snoring	3 (7.9)	43 (7.4)	NS	18 (36.0)	90 (18.0)	0.002
Sleep duration ≤5 h	4 (10.5)	40 (6.9)	NS	8 (16.0)	30 (6.0)	0.007
Sleep duration ≥9 h	3 (7.9)	14 (2.4)	0.035	1 (2.0)	7 (1.4)	NS
DIS	1 (2.6)	43 (7.4)	NS	8 (16.0)	16 (3.2)	<0.001
DMS	6 (15.8)	68 (11.7)	NS	14 (28.0)	32 (6.4)	<0.001
Depression	4 (10.5)	87 (14.9)	NS	7 (14.0)	33 (6.6)	NS

Data are means ±SD or *n* (%). *n* = 1,170. DIS, difficulties initiating sleep; DMS, difficulties maintaining sleep.

sleep were associated with new diabetes in men in the age-adjusted model.

After adjusting for age and other relevant factors, including difficulties initiating sleep, difficulties maintaining sleep, and deviant sleep duration in multivariate models, the positive association between obesity and new diabetes in women remained statistically significant. The multivariate RR for developing diabetes was increased in men living alone, in subjects who were obese, in subjects having difficulties maintaining sleep, and in subjects reporting short sleep duration at baseline. The influence of difficulties initiating sleep in women and long sleep duration in men could not be calculated because only one woman with new diabetes reported difficulties initiating sleep and only one man reporting new diabetes reported long sleep duration at baseline.

CONCLUSIONS — Our data suggest that difficulties maintaining sleep and short sleep duration are associated with incident diabetes in men. Their association with diabetes persists after adjustment for age, hypertension, snoring, BMI, depression, and other relevant factors in multivariate analyses. The association among difficulties maintaining sleep, short sleep duration, and diabetes may be mediated through several potential mechanisms, including sympathetic overactivity and activation of the hypothalamic-pituitary-adrenal axis. It has been hypothesized that poor sleep is the result of a state of emotional arousal (9), and the activity of the stress system has been found to relate positively to the degree of objective sleep disturbance (28). The disturbance and curtailment of sleep have also been shown to have an impact on metabolic parameters. Insomniacs have been shown to have higher 24-h ACTH levels and cortisol secretion (8,29), elevated urinary catecholamine concentrations (12), and higher sleep-to-awake ratio for metabolic parameters (13). In an experimental study by Spiegel et al. (14), sleep debt had an impact on carbohydrate metabolism and endocrine function in young men. In the sleep-debt condition,

Table 2—*Relative risks of new diabetes in women according to self-reported variables at baseline*

Reported variable or symptom in 1983	Age-adjusted model*	Multivariate model including DIS and DMS†	Multivariate model including sleep duration ≤5 h and sleep duration ≥9 h†
Not married	1.0 (0.5–2.4)	0.9 (0.4–2.4)	1.0 (0.4–2.6)
Living alone	1.0 (0.4–2.8)	0.7 (0.1–3.1)	0.6 (0.1–2.8)
Hypertension	1.3 (0.6–3.0)	1.5 (0.6–3.9)	1.7 (0.6–4.4)
Obesity (BMI ≥30 kg/m^2)	6.9 (3.4–14.2)‡	5.8 (2.4–14.0)‡	5.9 (2.5–14.2)‡
Smoking	0.3 (0.07–1.2)	0.3 (0.03–2.0)	0.2 (0.03–1.8)
Alcohol use	0.7 (0.3–1.5)	0.9 (0.4–2.1)	0.9 (0.4–2.2)
Snoring	1.1 (0.3–3.7)	0.7 (0.1–3.1)	0.6 (0.1–2.9)
Depression	0.8 (0.3–2.3)	1.0 (0.3–3.2)	0.9 (0.3–2.9)
Sleep duration ≤5 h	1.5 (0.5–4.5)		1.8 (0.5–6.8)
Sleep duration ≥9 h	3.5 (0.9–13.0)		2.9 (0.6–15.0)
DIS	NA	NA	
DMS	1.4 (0.5–3.4)	1.8 (0.5–6.0)	

Data are RR (95% CI). *n* = 620. *Adjusted for age in 5-year strata. †Adjusted for age in 5-year strata, not married, living alone, hypertension, obesity (BMI ≥30), smoking, alcohol use, snoring, and depression. ‡Significant ($P < 0.05$) RRs. DIS, difficulties initiating sleep; DMS, difficulties maintaining sleep.

Table 3—*Relative risks of new diabetes in men according to self-reported variables at baseline*

Reported variable or symptom in 1983	Age-adjusted model*	Multivariate model including DIS and DMS†	Multivariate model including sleep duration ≤5 h and sleep duration ≥9 h†
Not married	0.5 (0.1–2.0)	0.3 (0.06–1.8)	0.3 (0.06–1.5)
Living alone	3.0 (1.4–6.2)‡	3.4 (1.4–8.4)‡	2.9 (1.2–6.8)‡
Hypertension	0.6 (0.2–1.7)	0.5 (0.1–1.9)	0.6 (0.2–1.9)
Obesity (BMI ≥30)	8.6 (3.9–18.9)‡	6.6 (2.6–16.9)‡	6.7 (2.7–16.4)‡
Smoking	1.0 (0.5–2.1)	0.9 (0.4–2.2)	1.0 (0.4–2.5)
Alcohol use	1.0 (0.6–1.8)	1.0 (0.5–2.0)	0.9 (0.5–1.8)
Snoring	2.7 (1.5–5.1)‡	1.6 (0.8–3.5)	1.9 (0.9–3.8)
Depression	2.5 (1.1–6.0)‡	0.6 (0.2–2.0)	1.3 (0.4–3.6)
Sleep duration ≤5 h	3.1 (1.3–7.2)‡		2.8 (1.1–7.3)‡
Sleep duration ≥9 h	NA		NA
DIS	7.0 (2.7–17.7)‡	2.4 (0.7–8.6)	
DMS	6.2 (3.0–12.9)‡	4.8 (1.9–12.5)‡	

Data are RR (95% CI). $n = 550$. *Adjusted for age in 5-year strata. †Adjusted for age in 5-year strata, not married, living alone, hypertension, obesity (BMI ≥30 kg/m^2), smoking, alcohol use, snoring, and depression. ‡Significant ($P < 0.05$) RRs risks. DIS, difficulties initiating sleep; DMS, difficulties maintaining sleep.

glucose tolerance was lower as were thyrotropin concentrations. Moreover, evening cortisol concentrations were raised, and the activity of the sympathetic nervous system was increased, indicating that sleep loss has an adverse impact on components of the metabolic syndrome.

Some epidemiological studies have been performed to investigate the relationship between sleep and incidence of diabetes. Nilsson et al. (16) recently reported that difficulties in falling asleep or regular use of hypnotics predicted future diabetes in middle-aged men. In a study of sleep duration and incident diabetes in women enrolled in the Nurses Health Study, Ayas et al. (17) found that in an age-adjusted model both long and short sleep duration increased the risk of incident diabetes diagnosis, but after adjustment in a multivariate model the risk was only increased for long sleepers. When they investigated only symptomatic cases of diabetes, both short and long sleepers had a modestly elevated risk in the multivariate model, and the authors suggested that sleep restriction may be an independent risk factor for developing symptomatic diabetes. In a prospective 8-year follow-up survey of male employees in Japan, Kawakami et al. (18) reported that men with a high frequency of difficulties initiating sleep or difficulties maintaining sleep had significantly higher ratios for type 2 diabetes after controlling for relevant factors. The present study explores the relationship between several aspects of sleep and incident diabetes prospectively in both sexes in the general population.

The strengths of the current study include the representativeness of the baseline sample and the high response rate. Variables were included in the analysis if they were considered relevant risk factors for the development of diabetes. Hypertension, habitual snoring, obesity, smoking, alcohol consumption, depression, and weight gain are considered independent risk factors for type 2 diabetes. An advantage is that both questionnaires used in our study contained several questions about sleep, giving us an opportunity to investigate different aspects of sleep (habits, problems, duration of sleep, and perceived sleep need) in relation to incident diabetes.

One limitation is that we were not able to control for some important and well-known risk factors because we had no information at baseline, e.g., family history of diabetes and physical inactivity. Another limitation is that information about sleep, other potential risk factors, and diabetes were self-reports. However, self-reports of sleep are the measures most widely used in community-based epidemiological surveys, and there is evidence that subjective evaluations correlate with objective laboratory data (30,31). Short sleep was defined as sleeping ≤5 h per night and long sleep as sleeping ≥9 h per night to be able to compare our results with the findings reported by Ayas et al. (17). Also, some misclassification of diabetes is likely, and it is reasonable to assume that some subjects reporting no diabetes have undiagnosed diabetes. Studies have, however, demonstrated that self-reports of diabetes have high accuracy and that self-reports provide a useful estimate for measures of population prevalence of diabetes (32,33). Although the number of subjects with diabetes in this study was low, the prevalence is near to that in other epidemiological surveys (34,35). One obvious limitation is the small sample size and cell size, suggesting the need for cautious interpretation of these findings. However, our results are in line with previous studies indicating that both sleep disturbances (16,18) and short sleep duration (17) are related to incident diabetes. It is a fact, however, that diabetes is not an inevitable component or consequence of insomnia in the sense that a majority of subjects with insomnia do not have diabetes and will not develop diabetes.

An important question concerns whether researchers have either adjusted for or ruled out depression as a confounder in studies on the association between poor sleep and morbidity. In the present study the occurrence of depression was based solely on participants' responses to a single question about feeling depressed. However, in a review, Schade et al. (36) found that brief instruments perform about as well as longer questionnaires for identifying depression in the general population, and the value of single-item depression screening has previously been established (37,38). In the age-adjusted model depression was associated with incident diabetes in men, but in the multivariate models it was no longer statistically significant, reflecting a confounding effect of other variables included. Also, snoring in men was associated with new diabetes in the age-adjusted model but did not remain significant in the multivariate models. In contrast to Al-Delaimy et al. (39), we found no significant association between reported snoring in women and incident diabetes.

In the present study, obesity was a risk factor for incident diabetes for both women and men in the multivariate adjusted models. Obesity is a well-known risk factor for insulin resistance and type 2 diabetes (40,41). Subjects with new diabetes lost weight during the follow-up period in contrast to those not developing diabetes. In this longitudinal study, we lack knowledge about when events occurred. It is reasonable to assume that when diabetes was diagnosed subjects

were encouraged to make lifestyle changes, including diet and physical activity, and these could most likely have resulted in weight loss among those in whom diabetes was diagnosed. Living alone predicted new diabetes in men. Social isolation has previously been found to be related to morbidity and mortality (42).

Reporting difficulties maintaining sleep or sleep duration of ≤5 h increased the risk of new diabetes in men. Men with new diabetes reported shorter sleep time and lower SSI at baseline than men who did not develop diabetes. Of 38 men with sleep time ≤5 h only 3 reported sleep need of ≤5 h. None of these three men developed diabetes, indicating that all men reporting sleep time ≤5 h with future diabetes had insufficient sleep.

We found no relationship between sleep variables and future diabetes in women. A lower risk for physical morbidity and mortality related to sleeping difficulties in women has been shown in other epidemiological surveys (2,43). Several theories of sex differences in consequences of insomnia have been presented. There are biological differences including genetics and sexual hormones that affect sleep. Differences between men and women in the perception and evaluation of symptoms and symptom-reporting behavior have been found, and sex differences in stress and reaction to stress have been reported (44). In the present study, an association between sleep disturbances and incident diabetes was probably easier to demonstrate in men because of the higher incidence of diabetes in men. Furthermore, there was a lower prevalence of sleep problems in men. Difficulties initiating sleep in women were associated with nonresponse, which might have lead to an underestimation of this as a risk factor for future diabetes. Results from the Nurses Health Study revealed that short (≤5 h) and long (≥9 h) sleep in women were associated with future diabetes, but after controlling for confounders the association remained significant only for long sleepers (17). In this study, women developing diabetes reported long sleep at baseline more often, and in multivariate analyses including BMI the relative risk was 2.9, but the risk did not reach significance.

The most common and detrimental complication of diabetes is cardiovascular disease. Previously we have demonstrated that difficulties initiating sleep are predictive of death from coronary artery disease in men (45). The result of this study provides additional evidence linking disturbed or shortened sleep to long-term adverse health effects in men.

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