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Sleep disturbance is associated with cardiovascular and metabolic disorders

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SUMMARY

Existing research has demonstrated associations between sleep duration and obesity, diabetes, cardiovascular disease and mortality. Sleep disorders research has shown that sleep apnoea, insomnia and other sleep disorders confer risk for cardiometabolic disease, particularly in the presence of reduced sleep duration. The aim of the present study was to examine the associations between general sleep disturbance, operationalized as ‘difficulty falling asleep, staying asleep, or sleeping too much’ as measured in a large, nationally representative sample, and self-reported history of myocardial infarction, stroke, coronary artery disease, diabetes and obesity. Data from the Behavioral Risk Factor Surveillance System were analysed. Complete data were available for 138 201 individuals. A hierarchical logistic regression analysis examined associations before and after adjustment for demographic, socioeconomic, medical and psychological factors. After adjusting for demographic, socioeconomic and health risk factors, sleep duration was associated with obesity [odds ratio (OR) = 1.18, $P < 0.0005$], diabetes (OR = 1.18, $P < 0.005$), myocardial infarction (OR = 1.36, $P < 0.0005$), stroke (OR = 1.22, $P < 0.05$) and coronary artery disease (OR = 1.59, $P < 0.0005$). In fully adjusted models that included physical health, significant relationships remained for obesity (OR = 1.14, $P < 0.0005$), myocardial infarction (OR = 1.23, $P < 0.005$) and coronary artery disease (OR = 1.43, $P < 0.0005$). Sleep disturbance is a significant risk factor for obesity, diabetes, myocardial infarction, stroke and coronary artery disease, and effects for obesity, myocardial infarction and coronary artery disease are the most robust after adjustment. This study demonstrates that sleep disturbance is a novel risk factor that is potentially modifiable. Future research should determine whether sleep intervention could reduce the cardiometabolic consequences of sleep disturbance.

Keywords

cardiovascular disease; diabetes; myocardial infarction; obesity; sleep; stroke

INTRODUCTION

Epidemiological studies exploring the relationship between habitual sleep patterns and associated health outcomes have increased our understanding of the role of sleep in a number of important domains, including cardiometabolic risk and all-cause mortality (Grandner *et al.*, 2010a, c). Virtually all these studies investigated sleep duration as the only measure of sleep. However, more recent evidence demonstrates that aspects of sleep other than sleep duration are also important to investigate (Grandner *et al.*, 2010b; Troxel *et al.*, 2010).

A recent report from the Whitehall II study (Chandola *et al.*, 2010) found that the combination of sleep duration and sleep disturbance was a better predictor of coronary heart disease risk than sleep duration alone. The Whitehall II study was a major longitudinal study tracking the health of workers from 20 departments of the British civil service across 15 years. Although both sleep duration and sleep disturbance were associated with increased coronary heart disease risk, only sleep disturbance remained significant after adjustment for covariates. Upon closer examination, it appeared that there was an interaction between sleep disturbance and sleep duration, such that those with short sleep duration were at increased risk of coronary heart disease only if they also reported subjective sleep disturbance.

The Whitehall II data echo findings of Vgontzas *et al.* (2009), who reported that individuals with insomnia (one specific operationalization of sleep disturbance) were at increased risk for hypertension if they also reported short sleep duration (<5 h on average). Thus, in this study as well, an indicator of cardiovascular disease is associated with increased sleep disturbance in the context of short sleep duration.

Other studies have examined sleep disturbance (broadly defined) as a predictor of cardiometabolic risk. Tasali *et al.* (2008) showed that selective slow wave sleep suppression (as a model of disturbed physiological sleep without reduction in sleep duration) resulted in impaired insulin sensitivity and reduced glucose tolerance. At the epidemiological level, a recent study by Troxel *et al.* (2010) found that in 812 healthy adults, individuals with self-reported difficulty falling asleep, loud snoring and / or unrefreshing sleep were at increased risk of developing metabolic syndrome, as well as specific metabolic risk factors, including hyperglycaemia and low high-density lipoprotein cholesterol. This suggests that self-reported sleep complaints can have predictive power relative to cardiometabolic health outcomes.

The current study aims to extend these findings by exploring several cardiometabolic risk factors and focusing on perceived sleep quality which is a valuable and sensitive estimate of suboptimal sleep, rather than sleep duration. A secondary analysis of data gathered by the Behavioral Risk Factor Surveillance System data was collected by the Centers for Disease Control and Prevention in 2006. These data were analysed to explore whether sleep symptoms (assessed broadly) were significant independent predictors of self-reported (i) obesity, (ii) diabetes history, (iii) myocardial infarction history, (iv) coronary artery disease history and (v) stroke history.

METHODS

Participants

Data from the 2006 Behavioral Risk Factor Surveillance System (BRFSS) (Centers for Disease Control, 2007a) were used for this analysis. A total of 138 201 individuals provided complete data. The BRFSS is an annual, state-based, random-digit-dialled telephone interview survey of adults aged 18 years from all over the United States conducted by the

Centers for Disease Control and Prevention. It is the world's largest telephone survey, designed to monitor health-related behaviours in the general population. The overall response rate (completed interviews relative to total eligible households) varied across states, with a mean of 41.1%, median of 40.5% and range of 20.5% (Georgia) to 72.5% (Puerto Rico). The completion rate (number of interviews completed relative to the number of interviews completed, terminated and / or refused) also varied across states, with a mean and median of 78.1% and a range of 66.3% (California) to 92.5% (Puerto Rico).

To increase the generalizability of results and mitigate any response bias, each participant was assigned a weight to be used in analysis. Thus, even though the sample is, by the nature of the sampling scheme, not representative of the general population, all analyses are adjusted so that biases in the sample do not contaminate results. The process of determining participant weighting is discussed in more detail in the BRFSS documentation (Centers for Disease Control, 2007b). In brief, each weight is calculated using a combination of: (i) a weight which accounts for differences in the basic probability of selection among subsets of regions delineated by combinations of area code and telephone prefix, (ii) a weight which adjusts for non-coverage and non-response, forcing the sum of all weighted frequencies to equal population estimates for that region, based on age, sex and race / ethnicity, (iii) the number of residential telephone lines in the participant's home and (iv) the number of adults in the participant's household. Thus, although the sample that was aggregated is not representative of the general population, each participant's weight assures that all results are maximally generalizable, accounting for any non-coverage and / or non-response based on geographic region, as well as sociodemographic categories of age, sex and ethnicity.

Measures

Obesity was estimated by calculating body mass index (BMI) based on self-reported estimates of weight and height and categorizing volunteers as obese if BMI was ≥ 30 . Diabetes was assessed with the item: 'Have you ever been told by a doctor that you have diabetes?' Responses were categorized as 'yes' or 'no'. Cardiovascular outcomes assessed with a series of questions which began: 'Has a doctor, nurse, or other health professional ever told you that you had any of the following?' The following conditions were listed: (i) 'heart attack, also called a myocardial infarction', (ii) 'angina or coronary heart disease' and (iii) 'stroke'. Participants answered 'yes' or 'no'.

Participants also answered a question on sleep disturbance: 'Over the last 2 weeks, how many days have you had trouble falling asleep or staying asleep or sleeping too much?' Answers ranged from 0 to 14. However, the distributions were bimodal, with peaks at 0 and 14. Thus, sleep disturbance was dichotomized into those who report complaints ≥ 6 days and those who report complaints < 6 days out of 14. This is consistent with other classification approaches, where a frequency of three or more events per week has been used to denote abnormality (Jansson-Frojmark and Linton, 2008).

Covariates used to adjust for demographic and socioeconomic factors included age, sex, race / ethnicity (white, black / African American, other), education (less than high school, high school graduate, some college, college graduate), income level ($< \$10\,000$ pre-tax income per year, \$10 000– 15 000, \$15 000–20 000, \$20 000–25 000, \$25 000–35 000, \$35 000–50 000, \$50 000–75 000, $> \$75\,000$), employment (employed, self-employed, retired, student, homemaker, unemployed < 1 year, unemployed > 1 year, unable to work), marital status (married, in a relationship, never married, divorced, separated, widowed) and census region (South, West, Midwest, Northeast). Previous analyses of these data at the national level have found that age, gender, education, employment, marital status and income are significant predictors of sleep complaint in this sample (Grandner *et al.*, 2010b).

Covariates used to adjust for risk include physical health (number of days out of last 30 where physical health was not good), mental health (number of days out of past 30 that mental health was not good), access to health insurance (yes or no), access to health care (could not see a doctor at some point in the past year due to finances), smoking history (smoked 100 cigarettes in life-time) and alcohol use (average number of drinks per month). BMI was included as a covariate for all analyses except those examining obesity as an outcome.

Statistical analyses

Complete-case analysis was implemented; only participants who provided complete data were included for analysis. We conducted a series of logistic regression models for BMI and each of the four dichotomous outcomes of diabetes, myocardial infarction, coronary artery disease and stroke. All sampling was weighted appropriately for representativeness, using weighting scores developed specifically for BRFSS 2006. The odds ratios (ORs) and 95% confidence intervals (CIs) were estimated among groups relative to a preselected reference. For the logistic regression we present alcohol, mental health and physical health as drinks / days per week, rather than per month, for improved interpretation. Age is modelled in 5-year increments. Analyses were performed using STATA software version 11 (StataCorp, College Station, TX, USA). All statistical tests were two-tailed. Statistical significance was set at the $P < 0.05$ level. A total of four separate models were tested, to evaluate (i) unadjusted associations between sleep disturbance and the outcome, (ii) associations adjusted for social and demographic factors, (iii) associations adjusted for social and demographic factors as well as other health risk factors and (iv) associations adjusted for social and demographic factors as well as health risk factors and physical health.

RESULTS

Unweighted subject characteristics are reported in Table 1 (weighted values represent census data). The mean age of the sample was 48.8 [standard deviation (SD) = 15.2].

Results of logistic regression analyses are presented in Table 2. Sleep disturbance was a significant independent predictor of obesity in unadjusted analysis (model 1: OR = 1.35, $P < 0.0001$), and this relationship was maintained in analyses adjusted for sociodemographic factors (model 2: OR = 1.27, $P < 0.0001$) as well as these and other health risk factors (model 3: OR = 1.18, $P < 0.0001$). When physical health was also controlled for (model 4), the relationship was also significant (model 4: OR = 1.14, $P = 0.0004$). Sleep disturbance was also an independent predictor of diabetes in unadjusted analyses (model 1: OR = 1.54, $P < 0.0001$), and this relationship was maintained in analyses adjusting for sociodemographic factors (model 2: OR = 1.30, $P < 0.0001$) and was significant in a model that included these as well as other health risk factors (model 3: OR = 1.18, $P = 0.0015$). With the inclusion of physical health, sleep disturbance was not a significant predictor of diabetes (model 4: OR = 1.08, $P = 1.301$).

Regarding cardiovascular disease, sleep disturbance was a significant predictor of myocardial infarction (OR = 1.80, $P < 0.0001$), coronary artery disease (OR = 1.98, $P < 0.0001$) and stroke (OR = 2.02, $P < 0.0001$) in unadjusted analyses (model 1). In analyses adjusted for sociodemographic factors (model 2), sleep disturbance was still a significant predictor of myocardial infarction (OR = 1.57, $P < 0.0001$), coronary artery disease (OR = 1.80, $P < 0.0001$) and stroke (OR = 1.45, $P < 0.0001$). In analyses adjusted for both sociodemographic and other health risk factors, sleep disturbance remained a significant independent predictor of coronary artery disease (OR = 1.59, $P < 0.0001$), as well as myocardial infarction (OR = 1.36, $P < 0.0001$) and stroke (OR = 1.22, $P = 0.0157$). With the inclusion of physical health (model 4), sleep disturbance was still a significant independent

predictor of myocardial infarction (OR = 1.23, $P = 0.0032$) and coronary artery disease (OR = 1.43, $P < 0.0001$). In model 4, sleep disturbance was not a significant predictor for stroke (OR = 1.11, $P = 0.1797$).

DISCUSSION

The present study examined 2006 BRFSS data regarding subjective sleep disturbance as an independent predictor of cardiometabolic risk factors. In unadjusted analyses, sleep disturbance was related significantly to obesity, diabetes, coronary artery disease and previous myocardial infarction and stroke. After adjusting for demographic, socioeconomic and health risk covariates, all these relationships remained significant. When physical health was included in the model, however, associations with diabetes and stroke were rendered non-significant. These findings also suggest that both the relationship between sleep disturbance and stroke and sleep disturbance and diabetes may be better explained by associations with physical health. As physical health may impact the validity of inferences made about cause and effect or modify this relationship, future studies should incorporate this variable in analysis.

These findings support previous epidemiological studies that have shown repeatedly that sleep patterns such as short or long sleep duration are associated with a number of cardiometabolic outcomes, including obesity, diabetes, hypertension, hypercholesterolaemia, myocardial infarction and stroke. These findings have been examined relative to sleep quality in the past, as several studies have found associations between disturbed sleep at night and negative health outcomes (Gangwisch, 2009). These findings extend those previous studies by (i) simultaneously exploring several cardiometabolic risk factors in a nationally representative sample and (ii) focusing on perceived sleep quality, rather than sleep duration.

That this study found a significant relationship between subjective sleep disturbance and obesity, even after adjusting for a wide array of demographic, socioeconomic, medical and psychological covariates, is not surprising, given that previous studies have established that sleep and weight regulation are coupled in many ways (Nielsen *et al.*, 2010). Cross-sectional studies often find associations between sleep duration and sleep quality with body mass (Buxton and Marcelli, 2010; Rao *et al.*, 2009). In addition, prospective studies find that those with more disturbed sleep (short sleep duration or poor sleep quality) are at increased risk for development of weight gain and / or obesity (Magee *et al.*, 2010; Watanabe *et al.*, 2010). This study adds to this literature by virtue of (i) its large sample size, (ii) the inclusive nature of the sleep disturbance question and (iii) the wide array of potential confounding variables adjusted for in analyses.

In this study, subjective sleep disturbance was associated with diabetes after adjusting for demographic, socioeconomic and other health risk factors. However, this relationship was not maintained following adjustment for physical health. This is in contrast to numerous previous studies that have found associations between habitual self-reported short sleep duration and diabetes (Barone and Menna-Barreto, 2010; Buxton and Marcelli, 2010), as well as laboratory-induced short sleep and metabolic dysregulation suggestive of diabetes risk (Buxton *et al.*, 2010; Schmid *et al.*, 2011). Other studies have also found associations between sleep quality and diabetes—for example, several studies have linked sleep apnoea (a condition associated with intermittent night-time hypoxia, as well as severely fragmented sleep) with risk of diabetes (Pamidi *et al.*, 2010). Finally, a previous exploration in this sample (Grandner *et al.*, 2011) found an association between self-reported sleep disturbance and diabetes in both men and women, although this relationship (i) included different outcome and predictor variables and (ii) included fewer health-related covariates. In light of

these previous studies, the relationship between vague sleep complaints and diabetes probably conflates many possible pathways and causes of poor sleep, which are associated differentially with diagnosis of diabetes.

Regarding myocardial infarction, the present study found that there was a strong relationship in unadjusted analyses, and this relationship remained significant after adjusting for demographic and socioeconomic variables as well as other health variables. In addition to sleep apnoea, sleep duration has been associated previously with increased cardiovascular risk (Grandner *et al.*, 2010a) and increased risk of myocardial infarction in particular (Sabanayagam and Shankar, 2010), recent evidence suggests that it is the combination of short sleep duration and poor sleep quality that confers maximal risk (Chandola *et al.*, 2010). The present study extends the literature demonstrating sleep disturbances are associated with an increased risk of myocardial infarction.

Regarding stroke, the present study found a significant association between history of stroke and sleep disturbance in unadjusted analysis as well as adjustment for other health risk factors, but this finding was non-significant after adjusting for physical health. These results are in the context of a literature that has shown conflicting results—although a number of studies show a significant association between stroke and short sleep duration (Sabanayagam and Shankar, 2010) and sleep apnoea (Redline *et al.*, 2010), the strength of the association varies across studies. The associations between sleep disturbance and increased stroke remain to be clarified.

The findings for coronary artery disease were markedly different from those of the other cardiometabolic outcomes. Although the magnitude of the association with sleep disturbance is attenuated from a 98% increased risk to a 43% increased risk across models, this finding remains highly significant, even after adjustment for all covariates. These findings are supported partially by other studies that have found associations between sleep duration and related cardiovascular disease measures. Buxton and Marcelli (2010) found that both short and long sleep duration were significant predictors of cardiovascular disease in a similar sample with similar covariates. Another recent study by King and colleagues (King *et al.*, 2008) reported that short sleep duration was associated with incident coronary artery calcification. In addition, studies of sleep apnoea have shown that not only is sleep apnoea associated with an increased risk of coronary artery disease (Gottlieb *et al.*, 2010), but patients with coronary artery disease are at an increased risk of also having sleep apnoea (Shahar *et al.*, 2001). Thus, the present association may account for relationships of coronary artery disease with sleep duration and sleep-related breathing disorders, as well as potential unique risks associated with other types of sleep disruptions.

Limitations

Although this study has a number of methodological strengths, it also has some limitations. First, the sleep disturbance item is a compound question, assessing three different sleep-related complaints. This limits interpretation, as it potentially conflates different types of sleep disturbance—difficulty falling asleep most probably reflects insomnia, while difficulty staying asleep could reflect insomnia or sleep apnoea, and sleeping too much could reflect hypersomnia or narcolepsy. Furthermore, sleep disturbance may reflect depression. Not only do general sleep disturbance measures correlate with depression (Grandner *et al.*, 2006), but depression strongly predicts sleep disturbance according to this variable (Grandner *et al.*, in press). In an attempt to control for this bias, we included mental health as a covariate.

It is possible that the variable physical health may misrepresent the true role of the explanatory variable (i.e. measure of overall physical health). Because the question was

worded as the physical health of the subject in the past 30 days, this variable is subject to self-report (biased by social desirability to report better health) and recall bias (systematic error due to differences in accuracy of recall to memory of past events or experiences), which may not reflect accurately the true relationship underlying sleep disturbance and cardiometabolic disease. Thus, the present study is subject to misclassification bias, where there are inaccuracies in the methods of data acquisition, and it is possible to misclassify subjects. For example, all comorbidities in the present study are also self-reported as having been diagnosed, meaning that undiagnosed cases will also be misclassified.

Misclassification may also occur for variables such as physical health, in which patients who are not diagnosed with a physical health condition may believe they are in good health, and thus be misclassified. Misclassification may have had the one of several consequences: (i) it could have inflated effects, as presumably the most severe cases (which might exhibit the worst sleep) would have been diagnosed, (ii) it could have increased Type II error through the addition of increased variance among the non-diagnosed group and / or (iii) it could have biased responses, as those who are more likely to have been diagnosed might respond differentially to a question about symptoms that someone who has not.

Sleep disturbance as a general measure is not a typical metric employed in epidemiological analyses of sleep in the population; rather, self-reported sleep duration is used more commonly. The problem with sleep duration is that this does not consider any discrepancy between perceived sleep needed versus sleep obtained. The question included in the current study provides a valuable and sensitive estimate of suboptimal sleep (for whatever reason) in the general population. We purport that the item is sensitive because almost any problem associated with sleep—especially the most common (sleep insufficiency, sleep fragmentation, insomnia, and sleep apnoea)—could be captured by this question, which is advantageous in a large epidemiological survey. However, while this item has face validity, it has not been validated against standard measures of subjective or objective sleep.

Additionally, the sleep disturbance item is not specific to particular sleep disorders. This limits our ability to use responses to this item to describe symptoms or syndromes (e.g. insufficient sleep, long sleep, insomnia, sleep apnoea, daytime sleepiness). We do not know whether those that endorse sleep disturbance would meet diagnostic criteria for a sleep disorder, or to what degree either of these measures reflect sleep duration or sleep quality (as measured in a more traditional way). We believe, however, that the construct is probably externally valid, as it represents the vague complaints presented when people discuss sleep problems with health-care providers (Cole *et al.*, 2007). This is pertinent, as recognition for the importance of sleep and sleep disorders in public health continues to rise (Colten *et al.*, 2006). Broad population measures, which are often insensitive for specific diseases, are critical for public health policy, community services infrastructure and research planning.

The cross-sectional design (which might also be considered retrospective) of the present study limits our ability to comment on causality or on the cardiometabolic disease processes *per se* and can only suggest the presence of association. It is not possible to determine from such a design whether sleep disturbances preceded the cardiovascular disease, which might suggest a possible aetiological role, or whether sleep disturbance itself was in fact a result of the cardiovascular disease. The latter might be more likely, as the sleep item measured only the previous 2 weeks, whereas the cardiometabolic items probably reflect conditions lasting much longer. Only a large-scale longitudinal study could illuminate the role of sleep within an individual in the development of cardiovascular disease, obesity and / or diabetes.

CONCLUSION

In conclusion, the present study shows that in a nationally representative sample, sleep disturbances during at least three of seven nights on average are associated with increased

risk of having a history of heart attack, stroke, coronary artery disease, diabetes and obesity. After adjustment for demographic and socioeconomic covariates, relationships with myocardial infarction, coronary artery disease, diabetes and obesity remain. After adjustment for these factors, as well as other cardiometabolic risk factors, the associations with both obesity and coronary artery disease remain significant. These data suggest that sleep disturbance may be an important indicator of cardiometabolic disease risk. Future studies are needed to evaluate the temporal relationships among these measures and whether sleep intervention could reduce cardiometabolic consequences.

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Table 1

Weighted sample characteristics, expressed as percentage (%) for categorical variables and mean \pm standard deviation (mean \pm SD) for continuous variables

Variable	Categories	Distribution
Age	Mean \pm SD	45.0 \pm 16.8
Sex	Men (%)	50.86
	Women (%)	49.14
Race/ethnicity	White (%)	69.48
	Black/African American (%)	8.77
	Other (%)	21.75
Marital status	Married (%)	62.10
	Divorced (%)	9.59
	Widowed (%)	5.25
	Separated (%)	2.07
	Never married (%)	16.88
	Part of an unmarried couple (%)	4.11
Employment	Employed (%)	55.55
	Self-employed (%)	9.57
	Homemaker (%)	7.30
	Student (%)	4.06
	Retired (%)	14.22
	Unemployed >1 year (%)	1.75
	Unemployed <1 year (%)	2.91
	Unable to work (%)	4.64
Education	Less than high school (%)	10.89
	High school (%)	27.42
	Some college (%)	27.50
	College graduate (%)	34.19
Income	<\$10 000 (%)	4.86
	\$10 000–15 000 (%)	5.02
	\$15 000–20 000 (%)	6.79
	\$20 000–25 000 (%)	8.73
	\$25 000–30 000 (%)	12.35
	\$30 000–50 000 (%)	15.69
	\$50 000–75 000 (%)	17.78
	>\$75 000 (%)	28.78
Census region	South (%)	47.85
	West (%)	28.65
	Midwest (%)	21.00
	Northeast (%)	2.50
Poor mental health	Days/month (mean \pm SD)	3.43 \pm 7.43
	Computed days/week (mean \pm SD)	0.802 \pm 1.736

Variable	Categories	Distribution
Poor physical health	Days/month (mean \pm SD)	3.46 \pm 7.77
	Computed days/week (mean \pm SD)	0.809 \pm 1.816
Alcohol	Drinks/month (mean \pm SD)	12.6 \pm 47.7
	Computed drinks/week (mean \pm SD)	2.93 \pm 11.15
Smoking	No (%)	55.54
	Yes (%)	44.46
Health insurance	No (%)	15.92
	Yes (%)	84.08
Limited health-care access	No (%)	86.15
	Yes (%)	13.85
Obese	No (%)	74.16
	Yes (%)	25.84
Diabetes	No (%)	92.05
	Yes (%)	7.95
Myocardial infarction	No (%)	95.84
	Yes (%)	4.16
Stroke	No (%)	97.45
	Yes (%)	2.55
Coronary artery disease	No (%)	95.68
	Yes (%)	4.32

Table 2

Odds ratios (ORs) and confidence intervals (CIs) for obesity, diabetes and cardiovascular disease, predicted by sleep disturbance across four models[†]

Outcome	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Obesity	***1.35 (1.26–1.43)	***1.27 (1.19–1.36)	***1.18 (1.10–1.27)	***1.14 (1.06–1.22)
Diabetes	***1.54 (1.41–1.69)	***1.30 (1.18–1.43)	**1.18 (1.06–1.30)	1.08 (0.98–1.21)
Myocardial infarction	***1.80 (1.60–2.03)	***1.57 (1.37–1.79)	***1.36 (1.19–1.55)	**1.23 (1.07–1.41)
Coronary artery disease	***1.98 (1.78–2.21)	***1.80 (1.60–2.02)	***1.59 (1.40–1.80)	***1.43 (1.26–1.61)
Stroke	***2.02 (1.77–2.31)	***1.45 (1.24–1.68)	*1.22 (1.04–1.43)	1.11 (0.95–1.31)

 $P < 0.0005$;

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 $P < 0.005$;

*
 $P < 0.05$

[†]Model 1 includes sleep disturbance; model 2 includes sleep disturbance, age, sex, race/ethnicity, education, income, marital status, employment and census region; model 3 includes model 2 variables and mental health, health insurance, access to health care, smoking and alcohol; model 4 includes model 3 variables and physical health.