Insomnia Symptoms and Cardiorespiratory Fitness in Healthy Individuals: The Nord-Trøndelag Health Study (HUNT)

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Study Objectives: Previous studies have found an inverse association between insomnia and self–reported physical activity, but it is not clear whether insomnia is associated with cardiorespiratory fitness. Our aim was to investigate different insomnia symptoms in relation to the gold standard measure of cardiorespiratory fitness, i.e., peak oxygen uptake (VO_{2peak}).

Design: Cross-sectional population study.

Setting: Nord-Trøndelag County, Norway.

Participants: The group comprised 3,489 men and women who were free from cardiovascular or pulmonary diseases, cancer, and sarcoidosis and who did not use antihypertensive medication. They were included in the fully adjusted model when assessing all insomnia symptoms simultaneously.

Interventions: N/A.

Measurements and Results: For insomnia, the participants reported how often they had experienced sleep problems during the past 3 months, including difficulties falling asleep at night, repeated awakenings during the night, early awakenings without being able to go back to sleep, and daytime sleepiness. Response options were "never/almost never," "sometimes" or "several times a wk." To measure cardiorespiratory fitness, the participants were asked to walk or run on a treadmill with increasing speed and/or incline until exhaustion, and VO_{2peak} was recorded.

We found a modest inverse and graded association of the insomnia symptoms with VO_{2peak}. The association was independent of self-reported physical activity and was apparent for all insomnia symptoms except for early awakenings. We found a dose-response relation for a cumulative combination of insomnia symptoms and VO_{2peak} for experiencing zero, one to two, or three to four symptoms (P for trend < 0.001).

Conclusions: We found a modest inverse association of insomnia with VO_{2peak} independent of the conventional cardiovascular risk factors and self-reported physical activity.

Keywords: Cardiorespiratory fitness, insomnia, peak oxygen uptake, sleep

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INTRODUCTION

Insomnia is a self-reported condition that includes difficulty falling asleep or remaining asleep.[1,2] Insomnia is common in patients with cardiovascular disease and a growing body of evidence suggests that insomnia is associated with an increased risk of coronary heart disease,[3-5] but the underlying mechanisms for this association are largely unknown. However, several studies have reported that people with insomnia symptoms tend to have a lower level of physical activity,[6-9] which could represent a possible explanation for the increased risk of coronary heart disease in these individuals.

Insomnia could also be inversely associated with cardiorespiratory fitness because its major determinant is physical activity. However, so far only two relatively small studies have assessed the association between sleep and cardiorespiratory fitness using exercise tests.[10,11] Whereas physical activity corresponds to any bodily movement produced by skeletal muscles

that results in energy expenditure, cardiorespiratory fitness refers to the maximum ability of the circulatory system to supply and extract oxygen during heavy dynamical work with large muscle groups. Both measures are inversely associated with cardiovascular disease morbidity and mortality,[12,13] but it has recently been shown that peak oxygen uptake (VO_{2peak}), the gold standard measure of cardiorespiratory fitness, is a stronger determinant of cardiovascular disease risk and longevity than measures of physical activity.[13-16]

Our aim was to investigate the association of different symptoms of insomnia with VO_{2peak}, in a healthy group of men and women. In our large population-based study we could also take into account the effects of established cardiovascular risk factors, determinants of VO_{2peak} and psychologic distress.

METHODS

Data Collection

The adult population of Nord-Trøndelag County in Norway was invited to participate in the third wave of the county-wide health survey "Helseundersøkelsen i Nord-Trøndelag" (HUNT-3) between October 2006 and June 2008. Approximately 51,000 participated (54% of those invited). In the study, information was collected by self-administered questionnaires, clinical measurements, and blood samples. Thus, the self-reported information includes health status; use of tobacco, alcohol, and coffee; responses to some dietary items; use of

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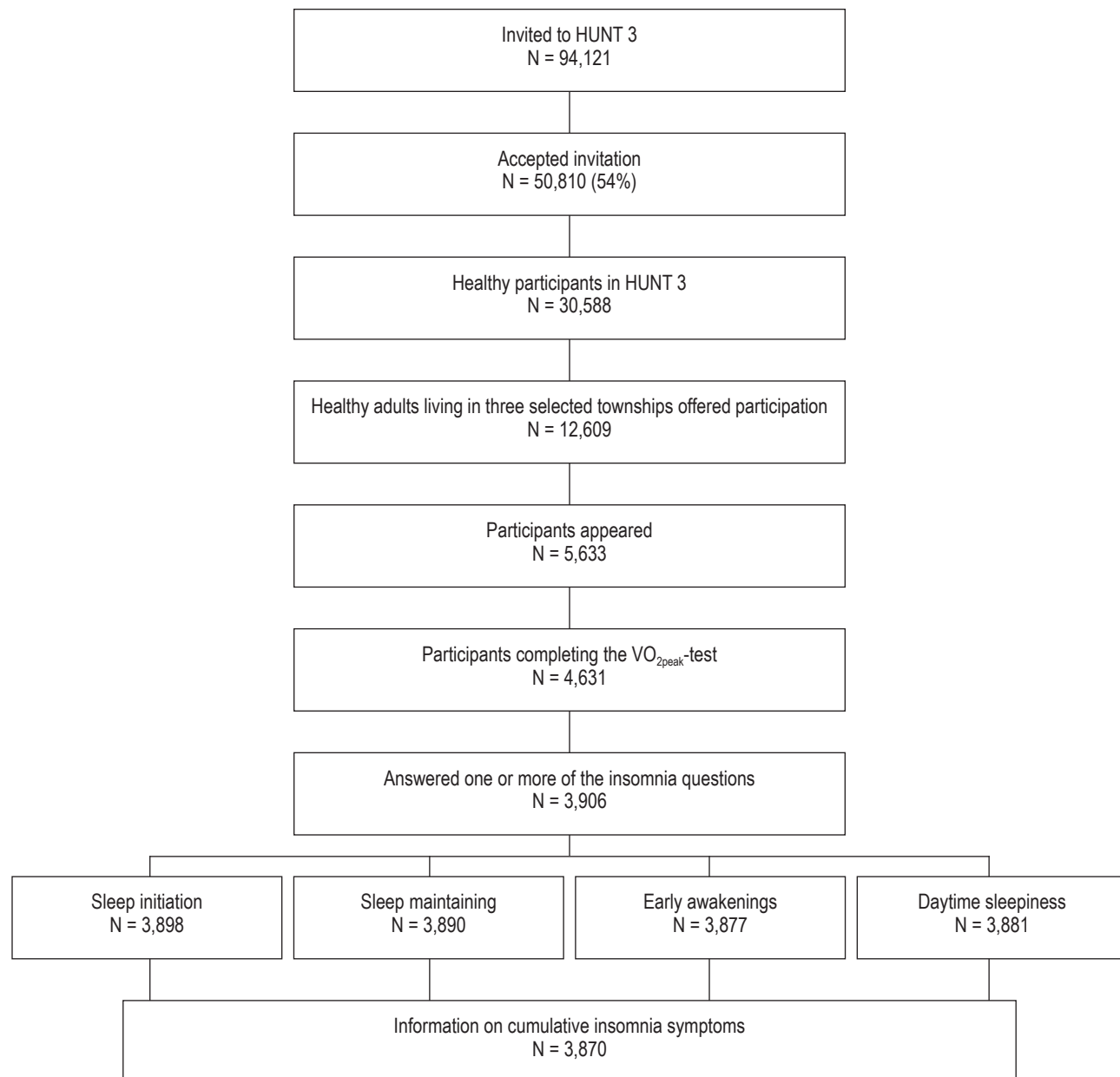
Figure 1—Selection process flow chart.

medication; and information on sleep, physical activity, education, and work history. Anthropometry, including measurements of height, weight, and waist and hip, was recorded, and blood pressure and serum lipids, including total and high-density lipoprotein (HDL) cholesterol, were measured.

Among the participants in HUNT-3, 30,513 were free from known cardiovascular or pulmonary diseases, cancer, and sarcoidosis and did not use antihypertensive medication at baseline, and were potentially eligible for a separate fitness study. Among them, 12,609 participants were residents in the three townships that were selected for the fitness study, and these participants were invited to the fitness study. A total of 4,631 participants accepted the invitation and completed the fitness test, which measured VO_{2peak}. The participants also responded to a physical activity questionnaire. The process of selecting the participants is illustrated in Figure 1.

Insomnia

The HUNT-3 questionnaire included nine questions about sleep. The participants answered how often during the past 3 months they had experienced difficulties falling asleep at night, repeated awakenings during the night, early awakenings without being able to go back to sleep, loud snoring, stopping to breath while asleep (sleep disordered breathing), sweating while asleep, daytime sleepiness, waking up with a headache, and having an uncomfortable feeling in the legs. The response categories were "never/almost never," "sometimes" or "several times a wk."

In total, 3,870 participants (83.4%) answered all the insomnia questions. The separate response rates for the questions about difficulties falling asleep at night, repeated awakenings during the night, early awakenings without being able to go back to sleep, and daytime sleepiness were 84.2% (n = 3,898),

84.0% (n = 3,890), 83.7% (n = 3,877), and 83.8% (n = 3,881), respectively. These response rates largely reflect the overall response rate of the HUNT-3 questionnaire that included the insomnia questions.

Peak Oxygen Uptake

Before the exercise test, the participants were briefly instructed about the treadmill test, and had 10 min of warming up at a moderate intensity during which they achieved light sweating and a modest shortness of breath, but did not reach subjectively ascertained exhaustion. Before getting on the treadmill (DK City, DK7830, Taichung, Taiwan), a heart rate monitor (Polar S610 or RS400, Polar, Kempele, 8 Finland) was fitted to each participant's chest and a mask (Hans Rudolph V, Shawnee, Kansas, USA) was fitted to the face.

Portable ergospirometry (Metamax II, Cortex Biophysic Gmbh, Leipzig, Germany) connected to a personal computer was used to measure the cardiorespiratory variables continuously. The test equipment was calibrated routinely by trained personnel. The participants were requested to walk or run on the treadmill at an increasing, individually adjusted speed and/or incline until exhaustion. When the oxygen uptake did not increase more than 2 mL/kg/min despite increased incline or speed, maximum oxygen uptake (VO_{2max}) was considered achieved. As a secondary criterion, the respiratory exchange ratio (i.e., the ratio of carbon dioxide output to oxygen uptake measured at external respiration) should exceed 1.05 to indicate a high level of effort. When the participant reached exhaustion, but not both criteria for VO_{2max}, the term VO_{2peak} was used. Because a considerable proportion of the participants (12.6%) did not achieve the criteria for VO_{2max}, the term VO_{2peak} is used throughout this article.

Physical Activity

The participants answered a questionnaire about weekly physical activity that included questions about frequency, intensity, and duration. The frequency question was stated as "How often do you exercise?" with the response options "Never," "Less than once a wk," "Once a wk," "Two to three times a wk" or "Almost every day." The question related to intensity was stated as "How hard do you exercise?" with the response options "No sweat or heavy breathing," "Sweat and heavy breathing," or "Push myself to exhaustion." Duration of the exercise was stated as "How long does each session last?" with the response options "Less than 15 min," "Between 15 and 29 min," "Between 30 and 60 min," or "More than 60 min." Frequency, intensity and duration were combined to form a physical activity index. We recoded the frequency scale to approximate number of times per wk (i.e., "0," "0.5," "1," "2.5," or "5"), the intensity scale to "1," "2," or "3," and the duration scale to the approximate number of hr per session (i.e. "0.10," "0.38," "0.75," and "1.00"). The physical activity index was the product of the recoded frequency, intensity, and duration scales. This method of calculating physical activity level has been reported and validated previously.[17]

Clinical Information

Clinical information on resting heart rate, weight, height, and blood pressure was collected by nurses. Resting heart rate was defined as beats per min after 10 min of rest in a dimly lit room. Systolic and diastolic blood pressure was measured three times (Dinamap 845XT Criticon) and the average of the second and third measurement was used in the analysis. Height was measured to the nearest 1 cm and weight to the nearest 0.5 kg. The participants were wearing lightweight clothing and no shoes during these measurements. Body mass index (BMI) was calculated as weight (in kilograms) divided by height squared (in meters).

Sociodemographic (i.e., sex, age, education level, and marital status) and lifestyle factors (i.e., smoking and alcohol intake) were collected by questionnaires. The participants were also asked if they were currently experiencing body pain that had lasted for more than 6 months.

Marital status was categorized into never married, married, or separated/divorced/widowed, and education was categorized into completion of primary and lower secondary school, upper secondary school, or university. The participants were defined as either never smokers, previous smokers, or current smokers. They were asked the question "Do you smoke?" with the alternatives "no, I have never smoked," "no, I have quit smoking," "yes, cigarettes occasionally," "yes, cigars/cigarillos/pipe occasionally," "yes, cigarettes daily," and "yes, cigars/cigarillos/pipe daily." If answering "no, I have never smoked" or "no, I have quit smoking" participants were categorized as never smokers or previous smokers, respectively. Current smoking was defined as currently smoking cigarettes/cigars or cigarillos/pipe, occasionally or daily. In relation to alcohol consumption, the participants reported how many glasses of beer, wine, and spirits they usually consumed over a 2-wk period. To accommodate a nonlinear relationship between alcohol consumption and cardiovascular health where light or moderate drinkers tend to be the healthiest and/or have the most favorable outcomes,[18] we categorized the participants into abstainers, light drinkers (zero to one drink per day), moderate drinkers (more than one but fewer than two drinks per day), or heavy drinkers (two or more drinks per day). One drink corresponds to a consumption of 10-15 g of alcohol.

Laboratory Measurements

A nonfasting blood sample was analyzed using a Hitachi 911 Autoanalyzer (Hitachi, Mito, Japan) at the Central Laboratory at Levanger Hospital. Within 2 hr, the blood was centrifuged at the site of the survey and placed in a refrigerator with a constant temperature of 4°C. The sample was sent to the laboratory the same day.

Total cholesterol and HDL cholesterol were analyzed by an enzymatic colorimetric method using reagents from Boehringer Mannheim (Mannheim, Germany). HDL cholesterol was measured after precipitation with phosphotungsten and magnesium ions.

Anxiety and Depression

To assess symptoms of anxiety and depression, the Hospital Anxiety and Depression Scale was used. The questionnaire consists of 14 questions (seven for anxiety and seven for depression) with a four-point scale ranging from zero (not at all) to three (very often). Responses are summed to provide separate scores for symptoms of anxiety and depression with possible

scores ranging from 0 to 21 for each scale. Higher scores indicate greater likelihood of depression or anxiety.[19] The Hospital Anxiety and Depression Scale has been found to be a useful tool in the assessment of symptom severity both in hospital settings and in primary health care.[20] The psychometric properties of the scale have been validated previously in the HUNT study.[21]

Statistical Analysis

Bivariate analyses of the data were done using chi-square tests or one-way analysis of variance for discrete and continuous variables, respectively. Multivariable analyses were performed using general linear models. We assessed the original response categories for each insomnia symptom (i.e., never/almost never, sometimes, several times a wk), and cumulative number of insomnia symptoms (i.e. zero, one to two, three to four symptoms) using indicator (dummy) variables in our regression models to reflect the categoric/ordinal nature of these variables. In the first model (Model 1), we adjusted for age and sex. In the second model (Model 2), we adjusted for age, sex, marital status, education, smoking, alcohol consumption, systolic and diastolic blood pressure, BMI, sleep disordered breathing, snoring, total serum cholesterol and HDL cholesterol, depression score, anxiety score, and chronic pain. In a third model (Model 3), we further adjusted for self-reported physical activity and resting heart rate. We calculated least square means of VO_{2peak} with corresponding 95% confidence intervals for each insomnia symptom. Participants with no insomnia complaints were the reference group. Analyses of trend were conducted separately to quantify the linear trend for the associations of these variables with peak oxygen uptake. We assigned a value from one to three to the insomnia variables representing "never/almost never," "sometimes," and "several times a wk," respectively, and treated these variables as continuous variables in our analyses of trend.

The insomnia symptoms were also dichotomized so we could assess their cumulative effects. Participants with the most frequent symptoms (i.e., those experiencing the symptom several times a wk) were defined as having the respective symptom. To test the cumulative effect of insomnia symptoms, we calculated the risk associated with increasing number of the dichotomized insomnia symptoms sleep initiation problems, repeated awakenings, and early awakenings (i.e. zero, one, two, and three). We did not include daytime sleepiness in the cumulative variable because it is not a core symptom of insomnia. In the analysis of the cumulative effects, we excluded participants with missing information on one or more of the insomnia variables.

As a sensitivity analysis we repeated the original analysis after excluding participants who reported symptoms of sleep disordered breathing, including cessation of breathing while asleep, and loud snoring several times a wk. In another sensitivity analysis we excluded participants who tended to experience waking up with a headache or nighttime sweating, in addition to participants who several times a wk stopped breathing and snored loudly while asleep. In further sensitivity analyses we excluded 67 participants with diabetes mellitus. We also excluded participants who did not answer all the insomnia questions and re-ran the analyses.

We assessed the association of insomnia symptoms and VO_{2peak} in analyses stratified by sex, age, BMI, education, and systolic blood pressure to investigate effect modification. We also performed formal tests for interactions between sex, age (i.e., younger and older than 50 yr), BMI (i.e., below and above 25 kg/m²), education (i.e., with and without a university degree), systolic blood pressure (i.e., below and above 130 mmHg), and insomnia.

All statistical analyses were conducted using STATA 11 for Windows (Stata Corp., College Station, TX).

RESULTS

Mean VO_{2peak} was 40.0 mL/kg/min (standard deviation 9.5 mL/kg/min) and the interquartile range was 13.2 mL/kg/min. Sex-specific estimates were 35.9 mL/kg/min and 44.3 mL/kg/min for women and men, respectively. Table 1 shows the frequency of the insomnia symptoms. Frequent awakenings several times a wk were twice as prevalent as problems with sleep initiation and early morning awakenings. In Table 2 we present the main characteristics according to cumulative number of insomnia symptoms. People with insomnia symptoms were older, more depressed, had higher BMI, lower physical fitness, and higher resting heart rate than participants without insomnia symptoms. Women were more likely to experience insomnia symptoms. In addition, participants who were separated, divorced, or widowed and participants with lower education level had an increased number of insomnia symptoms. People with insomnia symptoms also had lower VO_{2peak}. In Table 1, we also present the distribution of participants' characteristics according to each symptom. In general, the associations between these characteristics and the individual insomnia symptoms were similar to the associations found using the cumulative insomnia symptoms.

In Model 1, with adjustment for age and sex, there was a modest inverse and graded association between having difficulties falling asleep at night and VO_{2peak} (Table 3). After further adjustment for marital status, education, smoking, alcohol consumption, systolic and diastolic blood pressure, BMI, sleep disordered breathing, snoring, total serum cholesterol and HDL cholesterol, depression and anxiety score, and chronic pain (Model 2), the strength of the association somewhat weakened. Additional adjustment for the physical activity index and resting heart rate (Model 3) further attenuated the association. After adjustment for the potentially confounding factors in Model 2 and Model 3, there was also a graded inverse association between experiencing repeated awakenings during the night and VO_{2peak} (Table 3). For those who reported early awakenings, VO_{2peak} tended to be lower with increasing frequency of the symptom, but there was little statistical evidence for a linear trend.

For daytime sleepiness, we found an inverse association with VO_{2peak} that persisted after adjustment for the potential confounders in Model 2. With additional adjustment for the physical activity index and resting heart rate, the association was further attenuated.

We also used a combination of insomnia symptoms in the analysis, and found that increasing number of symptoms was inversely associated with VO_{2peak} in a dose-dependent manner (Table 4). Model 2 and Model 3 without adjustment for BMI provided essentially the same estimates (data not shown).

In a separate analysis, excluding 60 participants who reportedly stopping breathing while asleep and 489 participants reporting loud snoring several times a wk, the results remained essentially

Table 1—Characteristics of the study sample according to the insomnia symptoms

Variable	Sleep initiation problems				Frequent awakenings				Early awakenings				Daytime sleepiness			
	Never/almost never	Some-times	Several times/wk	P value	Never/almost never	Some-times	Several times/wk	P value	Never/almost never	Some-times	Several times/wk	P value	Never/almost never	Some-times	Several times/wk	P value
N (%)	2,024 (51.9)	1,559 (40.0)	315 (8.1)		1,477 (38.0)	1,784 (45.9)	629 (16.2)		2,054 (53.0)	1,507 (38.9)	316 (8.2)		1,150 (29.6)	2,308 (59.5)	423 (10.9)	
Age (yr)	48.4 (12.9)	50.1 (13.5)	52.9 (13.5)	< 0.001	46.1 (13.2)	51.1 (12.9)	52.5 (12.6)	< 0.001	46.3 (13.3)	52.7 (12.6)	53.7 (10.2)	< 0.001	52.5 (13.1)	48.9 (13.1)	44.0 (12.4)	< 0.001
BMI (kg/m²)	26.1 (3.5)	25.7 (3.6)	24.0 (3.7)	0.003	25.9 (3.5)	26.0 (3.5)	26.2 (3.8)	0.142	25.9 (3.6)	26.0 (3.5)	26.3 (3.5)	0.189	25.9 (3.4)	26.0 (3.5)	26.2 (4.4)	0.288
HADS anxiety score	3.0 (2.6)	4.3 (3.1)	5.8 (3.7)	< 0.001	2.8 (2.6)	3.9 (3.0)	5.4 (3.6)	< 0.001	3.0 (2.6)	4.3 (3.2)	5.4 (3.6)	< 0.001	2.7 (2.5)	3.9 (2.9)	6.0 (3.8)	< 0.001
HADS depression score	2.3 (2.3)	3.0 (2.7)	4.1 (3.3)	< 0.001	2.1 (2.3)	2.8 (2.6)	3.8 (3.1)	< 0.001	2.2 (2.3)	3.1 (2.7)	4.2 (3.1)	< 0.001	2.1 (2.2)	2.8 (2.6)	4.2 (3.3)	< 0.001
Diastolic BP (mm Hg)	74.1 (10.4)	73.0 (10.7)	71.6 (10.8)	< 0.001	73.2 (10.7)	73.8 (10.7)	73.2 (10.5)	0.193	73.1 (10.7)	73.7 (10.6)	74.3 (10.3)	0.099	74.3 (10.4)	73.3 (10.7)	71.9 (10.5)	< 0.001
Systolic BP (mm Hg)	128.1 (15.7)	127.5 (15.6)	126.2 (14.9)	0.099	127.0 (15.4)	128.6 (16.0)	127.2 (14.7)	0.012	126.9 (15.3)	128.6 (16.1)	128.5 (14.7)	0.003	130.4 (15.7)	127.2 (15.6)	123.3 (13.8)	< 0.001
Total cholesterol (mmol/L)	5.4 (1.0)	5.5 (1.1)	5.8 (1.1)	< 0.001	5.4 (1.1)	5.6 (1.1)	5.6 (1.0)	< 0.001	5.4 (1.1)	5.6 (1.1)	5.7 (1.0)	< 0.001	5.6 (1.0)	5.5 (1.1)	5.3 (1.0)	< 0.001
HDL cholesterol (mmol/L)	1.4 (0.3)	1.4 (03)	1.5 (0.4)	< 0.001	1.4 (0.3)	1.4 (0.4)	1.4 (0.4)	< 0.001	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	< 0.001	1.4 (0.4)	1.4 (0.3)	1.3 (0.3)	< 0.001
Physical activity index	3.7 (2.7)	3.7 (2.6)	3.4 (2.7)	0.247	3.7 (2.8)	3.7 (2.6)	3.6 (2.7)	0.587	3.6 (2.7)	3.8 (2.6)	3.5 (2.7)	0.186	3.8 (2.6)	3.7 (2.7)	3.6 (2.9)	0.343
Resting heart rate (beats/min)	58.8 (9.4)	59.5 (9.8)	60.4 (9.4)	0.010	58.6 (9.2)	59.5 (9.7)	59.8 (9.9)	0.007	59.3 (9.7)	58.9 (9.5)	59.9 (9.3)	0.227	59.4 (9.1)	58.9 (9.8)	60.3 (9.6)	0.023
VO₂peak (mL/kg/min)	40.9 (9.3)	39.0 (9.4)	35.4 (7.8)	< 0.001	42.0 (9.7)	38.7 (8.9)	37.0 (8.6)	< 0.001	41.0 (9.5)	38.4 (9.0)	37.4 (8.7)	< 0.001	39.5 (9.4)	39.8 (9.4)	39.8 (9.1)	0.562
Sex																
Women	45.2	58.5	71.1	< 0.001	46.2	54.9	60.4	< 0.001	50.3	54.9	55.4	0.014	49.9	53.0	56.5	0.048
Men	54.8	41.5	28.9		53.8	45.1	39.6		49.7	45.1	44.6		50.1	47.0	43.5	
Smoking																
Never	54.8	48.7	41.4	< 0.001	56.4	49.4	45.1	< 0.001	54.6	48.1	45.8	< 0.001	53.7	51.0	46.9	0.004
Previous	28.0	26.2	28.8		23.1	29.0	32.6		24.1	30.4	34.6		28.3	27.1	26.3	
Current	17.2	25.1	29.8		20.5	21.6	22.3		21.4	21.5	19.6		18.1	22.0	26.8	
Marital status																
Never married	23.6	24.4	20.7	< 0.001	28.2	21.6	19.0	< 0.001	27.9	19.5	17.1	< 0.001	18.9	24.3	34.0	< 0.001
Married	64.8	59.8	60.2		61.0	63.7	62.7		61.1	63.8	65.2		67.0	61.9	52.3	
Divorced/widowed	11.6	15.8	19.1		10.9	14.8	18.3		11.1	16.7	17.7		14.0	13.9	13.8	
SDB																
Never/almost never	91.1	94.4	91.8	0.007	93.0	92.8	90.2	0.169	92.7	92.6	90.5	0.598	94.3	92.3	88.4	< 0.001
Sometimes	7.1	4.4	6.9		5.6	5.9	7.4		5.7	6.1	7.3		4.9	6.4	6.5	
Several times/wk	1.8	1.3	1.3		1.4	1.4	2.5		1.6	1.4	2.2		0.8	1.3	5.1	
Snoring																
Never/almost never	51.8	60.5	54.1	< 0.001	58.4	53.8	52.4	0.026	57.4	53.5	49.7	0.034	57.2	54.2	55.5	< 0.001
Sometimes	33.1	30.3	32.8		29.6	33.6	32.9		30.3	33.7	34.9		32.5	33.0	25.1	
Several times/wk	15.1	9.3	13.1		12.0	12.6	14.7		12.3	12.8	15.4		10.3	12.7	19.4	
Alcohol intake																
Abstainers	16.0	17.6	16.6	0.426	16.1	16.5	18.4	0.761	17.4	15.0	20.0	0.366	15.4	15.6	25.2	< 0.001
Light drinkers	59.5	58.4	62.9		60.6	59.2	5.8		59.0	60.3	57.7		61.8	59.5	52.6	
Moderate drinkers	17.9	18.6	15.3		17.5	18.3	18.1		17.8	18.3	16.8		16.7	18.5	17.3	
Heavy drinkers	6.6	5.5	5.2		5.8	6.1	6.7		5.9	6.5	5.5		5.9	6.4	4.8	
Chronic pain																
No	76.4	68.8	50.8	< 0.001	80.8	71.3	49.3	< 0.001	76.9	67.5	54.2	< 0.001	76.7	71.9	54.3	< 0.001
Yes	23.6	31.2	49.2		19.2	28.7	50.7		23.2	32.5	45.8		23.3	28.1	45.7	
Education																
Primary	9.4	11.3	20.1	< 0.001	8.8	12.0	13.6	0.001	8.8	13.0	15.6	< 0.001	12.4	10.3	10.2	0.002
Secondary	51.0	51.6	55.6		51.0	52.3	51.8		50.4	52.3	56.2		54.9	50.7	48.8	
Tertiary	39.6	37.1	24.3		40.3	35.7	34.6		40.8	34.8	28.3		32.8	39.1	41.0	

BMI, body mass index; BP, blood pressure; HADS, Hospital Anxiety and Depression Scale; HDL, high-density lipoprotein; SDB, sleep disordered breathing; VO₂peak, peak oxygen uptake.

unchanged in all models (see Supplementary Tables S1 and S2). Additional exclusion of participants experiencing waking up with a headache or experiencing nighttime sweating resulted in no appreciable changes. Likewise, we did not observe any considerable differences when excluding 67 participants with diabetes mellitus (Supplementary Tables S3 and S4). Undertaking the analysis on participants who answered all the insomnia questions did not change the results (Supplementary Table S5).

We found no statistical evidence for effect modification of the association between insomnia symptoms and VO₂peak by sex, age, BMI, systolic blood pressure, or education, based on stratified analyses and by formal testing of possible interactions.

DISCUSSION

In this large population study, we found a modest inverse and graded association between insomnia symptoms and cardiorespiratory fitness, as indicated by peak oxygen uptake (VO₂peak). To the best of our knowledge, a similar analysis, using directly measured VO₂peak, has not been previously published. The association was largely independent of self-reported physical activity and it was apparent for all insomnia symptoms. By combining the symptoms in a cumulative manner, there was also an inverse dose-response association with VO₂peak.

Overall, the fitness study population attained higher levels of VO₂peak than participants in most of the other studies with comparable data.[22-26] There are no widely accepted reference values for VO₂peak, but others have reported mean sex-specific levels ranging from 32 mL/kg/min to 42 mL/kg/min in young women (i.e., age 20-29 yr) to 21 mL/kg/min to 26 mL/kg/min in older women (older than 69 yr) based on population data. Among young men, estimates have ranged from 38 mL/kg/min to 48 mL/kg/min, and to 25 mL/kg/min to 31 mL/kg/min in older men.[22-26] In another study of healthy people that may be similar to that of the participants of our study, VO₂peak levels were also similar to our findings.[27] Thus, VO₂peak was 33.0 mL/kg/min in women and 42.4 mL/kg/min in men. The difference between these levels and our study results seems to be attributable to differences in the older age groups.

Other cross-sectional population studies have assessed the association of some insomnia symptoms with self-reported physical activity and generally found an inverse association.[6-8] Only two studies have evaluated insomnia in relation to cardiorespiratory fitness.[10,11] Thus, in a study of 552 adolescent girls the 20-m shuttle-run test was used to estimate fitness, and girls who were classified as fit were more likely to report better sleep quality than other girls.[10] In another study of 291 female college

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Table 2—Characteristics of the study sample according to cumulative number of insomnia symptoms

		Cumulative insomnia symptoms				
Variable	n	0	1	2	3	P value
n	4,631	3,045	491	254	87	
Age (yr)	3,870	48.6 (13.2)	51.5 (13.3)	53.8 (11.6)	53.7 (11.3)	< 0.001
BMI (kg/m^2)	3,869	25.9 (3.5)	26.1 (3.8)	26.1 (3.8)	26.3 (4.1)	0.476
HADS anxiety score	3,862	3.3 (2.8)	4.9 (3.3)	5.7 (3.5)	6.6 (4.1)	< 0.001
HADS depression score	3,865	2.4 (2.5)	3.6 (2.9)	4.0 (3.0)	4.8 (3.5)	< 0.001
Diastolic BP (mmHg)	3,854	73.5 (10.5)	73.8 (11.2)	73.4 (10.7)	71.0 (8.8)	0.156
Systolic BP (mmHg)	3,867	127.7 (15.6)	128.0 (15.6)	127.7 (15.4)	124.9 (12.6)	0.388
Total cholesterol (mmol/L)	3,753	5.5 (1.0)	5.6 (1.1)	5.7 (1.0)	5.7 (1.0)	< 0.001
HDL-cholesterol (mmol/L)	3,753	1.4 (0.3)	1.4 (0.4)	1.5 (0.4)	1.5 (0.5)	0.002
Physical activity index	3,522	3.7 (2.7)	3.7 (2.6)	3.5 (2.5)	3.4 (3.2)	0.398
Resting heart rate (beats/min)	3,602	59.0 (9.6)	60.1 (9.7)	59.5 (10.0)	60.7 (8.7)	0.081
VO$_{2peak}$ (mL/kg/min)	3,870	40.4 (9.4)	38.0 (9.1)	36.2 (8.0)	35.1 (7.7)	< 0.001
Sex						< 0.001
Women	2,030	50.7	55.4	60.2	77.0	
Men	1,840	49.3	44.6	39.8	23.0	
Smoking						< 0.001
Never	1,959	53.3	44.1	41.4	50.6	
Previous	1,047	25.9	33.2	34.1	26.4	
Current	813	20.7	22.7	24.5	23.0	
Marital status						0.001
Never married	917	24.9	20.9	17.3	18.4	
Married	2,409	62.2	64.6	64.2	56.3	
Separated/divorced/widowed	535	13.0	14.5	18.5	25.3	
Sleep disordered breathing						0.267
Never/almost never	3,532	92.9	91.0	89.0	93.1	
Sometimes	229	5.6	6.9	8.9	4.6	
Several times a wk	60	1.4	2.1	2.0	2.3	
Snoring						0.022
Never/almost never	2,109	56.4	49.6	51.2	58.6	
Sometimes	1,255	31.6	33.3	34.7	31.0	
Several times a wk	487	12.0	17.2	14.1	10.3	
Alcohol intake						0.113
Abstainers	626	16.3	16.0	18.7	22.1	
Light drinkers	2,260	59.9	56.7	56.9	65.1	
Moderate drinkers	6,881	17.7	20.6	19.5	5.8	
Heavy drinkers	231	6.1	6.7	4.9	7.0	
Chronic pain						< 0.001
No	2,707	76.2	57.3	50.0	40.5	
Yes	1,086	23.8	42.7	50.0	59.5	
Education						< 0.001
Primary	423	10.0	12.9	17.0	18.6	
Secondary	1,990	51.5	49.1	56.9	57.0	
Tertiary	1,442	38.5	39.0	26.1	24.4	

BMI, body mass index; BP, blood pressure; HADS, Hospital Anxiety and Depression Scale; HDL, high-density lipoprotein; VO$_{2peak}$, peak oxygen uptake.

students, a 800-m run/walk test was used to estimate fitness, and there was a positive correlation between the test result and the total Pittsburg Sleep Quality Index score (Pearson correlation coefficient 0.43).[11] Also, they found that daytime sleepiness was more strongly correlated with cardiorespiratory fitness (Pearson correlation coefficient 0.43) than was sleep initiation (Pearson correlation coefficient 0.24).

We found that reporting frequent awakenings several times a wk was twice as prevalent as problems with sleep initiation and early morning awakenings. Several previous studies reported similar prevalence for all insomnia symptoms.[28-30] We speculate that sunlight during the night in summer and spring (due to the high latitude of Nord-Trøndelag County) could have facilitated repeated awakenings in our study population. However, some

Table 3—Least square means and 95% confidence intervals for the insomnia symptoms and VO_{2peak} (mL/kg/min)

	Model 1[a]		Model 2[b]		Model 3[c]	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
Sleep initiation problems						
Never/almost never	39.9	39.6 – 40.2	40.4	39.7 – 41.0	40.3	40.0 – 40.6
Occasionally	39.8	39.4 – 40.1	39.9	39.3 – 40.5	40.3	40.0 – 40.6
Several times/wk	38.3	37.5 – 39.0	39.1	37.5 – 40.7	39.3	38.6 – 40.0
P value for linear trend	0.003		0.012		0.089	
Repeated awakenings						
Never/almost never	40.3	39.9 – 40.6	40.9	40.1 – 41.7	40.6	40.3 – 40.9
Occasionally	39.5	39.2 – 39.9	39.8	39.5 – 40.2	40.1	39.8 – 40.4
Several times/wk	38.8	38.2 – 39.3	38.9	37.6 – 40.2	39.5	39.0 – 40.0
P value for linear trend	< 0.001		< 0.001		< 0.001	
Early awakening						
Never/almost never	39.7	39.4 – 40.0	40.4	39.7 – 41.0	40.3	40.1 – 40.6
Occasionally	39.8	39.5 – 40.2	39.8	39.2 – 40.4	40.1	39.7 – 40.4
Several times/wk	39.3	38.5 – 40.1	39.3	37.6 – 40.9	39.9	39.2– 40.6
P value for linear trend	0.723		0.789		0.171	
Daytime sleepiness						
Never/almost never	40.4	40.0 – 40.8	40.4	39.4 – 41.4	40.5	40.1 – 40.8
Occasionally	39.7	39.4 – 39.9	40.0	39.7 – 40.4	40.2	39.9 – 40.4
Several times/wk	38.1	37.5 – 38.8	39.5	38.0 – 41.0	39.7	39.1 – 40.3
P value for linear trend	< 0.001		0.002		0.046	

[a]Model 1 is adjusted for age and sex. [b]Model 2 is adjusted for age, sex, marital status, education, smoking, alcohol consumption, systolic and diastolic blood pressure, body mass index, sleep disordered breathing, snoring, serum total cholesterol, high-density lipoprotein cholesterol, depression score, anxiety score, and chronic pain. [c]Model 3 is adjusted for the same variables as in Model 2, and physical activity index and resting heart rate. CI, confidence interval.

Table 4—Least square means and 95% confidence intervals for the cumulative insomnia symptoms (sleep initiation problems, repeated awakenings and early awakenings) and VO2$_{peak}$ (mL/kg/min)

		Model 1[a]		Model 2[b]		Model 3[c]	
Insomnia symptoms	n	Mean	95% CI	Mean	95% CI	Mean	95% CI
0	3,045	39.9	39.7 – 40.2	40.2	40.0 – 40.4	40.4	40.1 – 40.6
1	491	39.0	38.4 – 39.7	39.6	39.0 – 40.1	39.8	39.2 – 40.3
2	254	38.5	37.7 – 39.4	39.3	38.5 – 40.1	39.2	38.5 – 40.0
3	87	38.8	37.4 – 40.3	39.7	38.6 – 41.3	39.8	38.4 – 41.1
P value for linear trend		< 0.001		0.020		0.005	

[a]Model 1 is adjusted for age and sex. [b]Model 2 is adjusted for age, sex, marital status, education, smoking, alcohol consumption, systolic and diastolic blood pressure, body mass index, sleep-disordered breathing, snoring, serum total cholesterol, and high-density lipoprotein cholesterol, depression score, anxiety score, and chronic pain. [c]Model 3 is Adjusted for the same variables as in Model 2, and physical activity index and resting heart rate. CI, confidence interval.

of the previous studies actually found a higher prevalence for frequent awakening than for sleep initiation or early morning awakening, which is in line with our results.[31,32]

Although acute sleep deprivation and insomnia are distinctly different conditions, it should be mentioned that a few small-scale experimental studies have measured VO_{2peak} in healthy volunteers to estimate the effect of acute sleep withdrawal on cardiorespiratory fitness.[33,34] The results showed that VO_{2peak} decreased after the loss of 3 hr of sleep in seven male cyclists,[33] with a gradual reduction in VO_{2peak} with increasing sleep deprivation during a 64-hr sleep deprivation period among 12 participants.[34]

In addition to the direct measurement of VO_{2peak}, we could also adjust for self-reported physical activity in the analysis of insomnia symptoms and cardiorespiratory fitness. Thus, we found that the association of insomnia with VO_{2peak} was independent of self-reported physical activity. VO_{2peak} measures a person's peak aerobic capacity, which is considered the most important determinant of aerobic and endurance performance.[35] Nevertheless, the association with physical activity is modest at the population level. Self-reported physical activity is more prone to misclassification than VO_{2peak}.[36] Such a misclassification can result in a weaker association with its correlates. In contrast, VO_{2peak} is a considered to be the gold standard measurement of cardiorespiratory fitness, which is determined by physical activity and other factors including genes.[37-39] Several studies have also proposed that VO_{2peak} is

more strongly associated with cardiovascular disease risk and survival than physical activity.[13-15]

Our results suggest that repeated awakenings were more strongly associated with VO_{2peak} (P for linear trend < 0.001) than sleep initiation, early awakenings, and daytime sleepiness. The tendency for lower VO_{2peak} with increasing severity of the insomnia seems clear, however, for all four insomnia symptoms (Model 3). Somewhat similar results were reported by Japanese investigators who found no clear association of early awakenings with self-reported physical activity, but an inverse association with the other symptoms.[7] Nevertheless, more research is needed to establish whether different insomnia symptoms have differential associations with cardiorespiratory fitness and physical activity.

Although the nature of the association between insomnia and VO_{2peak} remains unclear, there are several plausible underlying mechanisms for the observed inverse association. One possible explanation is that people who suffer from insomnia are less likely to engage in physical activity,[40] but it is also possible that a sedentary lifestyle could lead to poorer quality of sleep.[41] Moreover, insomnia may share some common risk factors with poor fitness or may affect VO_{2peak} via physiologic hyperarousal or metabolic changes.[42] Several studies have shown that insomnia is associated with increased body temperature,[43] increased heart rate,[44] increased metabolic rate,[45] and increased activity of the hypothalamic-pituitary-adrenal (HPA) axis,[46] all of which also are associated with physical inactivity in a similar fashion.[47] More recently it has also been reported that insomnia is associated with cardiovascular risk factors such as hypertension or diabetes,[48-50] both of which are correlates of cardiorespiratory fitness.[51,52]

Women are more prone to insomnia than men,[2] and there is a documented sex difference in peak oxygen uptake.[53,54] However, our study and previous studies have failed to provide evidence for any sex difference related to the association of insomnia symptoms with physical activity or cardiorespiratory fitness.[6,7]

Limitations

Despite the relatively large sample size, the population-based design, and the use of directly measured VO_{2peak}, the current study also has some limitations.

Most importantly, this study may be subject to bias because of self-selection due to the low participation rate (44.6%). However, almost all of those who were invited to the current study from the large HUNT study agreed to participate in the fitness test. Due to limited capacity at the test sites resulting in long lines, many potential participants chose to withdraw their participation from the study. Those who finally participated in the study could be healthier than those who quit or declined participation. A comparison of the participants in the fitness study with a healthy sample of the total HUNT population (i.e., free from cardiovascular or pulmonary diseases, cancer, or sarcoidosis) confirmed that the fitness participants did not considerably differ from other healthy HUNT participants although they had slightly lower mean weight (69.8 kg compared with 71.5 kg in women, and 85.6 kg compared with 86.2 kg in men), and BMI (25.4 compared with 26.1 in women, and 26.6 compared with 27.0 in men). In female fitness study participants, mean waist-to-hip ratio was 0.85 compared with 0.86, systolic blood pres-

sure was 123.5 mm Hg compared with 124.3 mm Hg, diastolic blood pressure was 69.7 mm Hg compared with 69.8 mm Hg, and cholesterol levels was 5.44 mmol/L compared with 5.52 mmol/L in the healthy HUNT population. In men, mean waist-to-hip ratio was 0.92 in both groups, whereas mean systolic and diastolic blood pressure was 131.9 mm Hg and 76.2 mm Hg in the fitness study population compared with 131.4 mm Hg and 75.4 mm Hg in the healthy HUNT population. Cholesterol levels were 5.48 mmol/L and 5.50 mmol/L in the two groups, respectively.[55]

The response rate to the insomnia questions was 83.4%, which largely reflects the overall response rate to the questionnaire with the insomnia items. Thus, a nonresponse bias specifically caused by avoidance of questions targeting insomnia is not likely in the current study.

The cross-sectional study design did now allow us to assess the direction of the association of insomnia with cardiorespiratory fitness. Although insomnia may also share some determinants with cardiorespiratory fitness, we adjusted for a large set of covariates in the analysis, and the association of insomnia symptoms with VO_{2peak} was largely independent of these covariates.

This study is based on self-reported measures of sleep, and validation with objective measures (i.e., by polysomnography) was not available. However, insomnia is not routinely evaluated by polysomnography,[56] and the condition is typically defined as "a self-reported condition which includes having difficulties falling asleep, or remaining asleep."[1,2] Thus, insomnia may be present even if a polysomnographic evaluation shows no sign of it.

Self-report is always prone to individual interpretation when no anchors are given and this approach does not allow quantitative or objective assessment of the degree of insomnia. However, there might also be some disadvantages with anchored questions. Insomnia is a subjective feeling and the same sleep problem might be perceived differently by different individuals. For example, lying awake in bed for 20 min might be a significant problem for some, whereas others might not be bothered by this. In contrast, our approach reflects the degree of subjective problems perceived by the individual.

Hormone replacement therapy has well-known positive effects on insomnia.[57] Regrettably, we did not have information on this variable in our study. We have, however, adjusted for strong correlates of hormonal replacement therapy such as age and socio-demographic characteristics and therefore our multi-adjusted estimates are not likely to be substantially confounded by the use of hormone replacement therapy among women entering menopause.

We also did not have information about ethnicity in our study. However, Nord-Trøndelag County in Norway has a very homogenous population with fewer than 3% non-Caucasians.[58]

Our study was performed in an apparently healthy, socio-economically homogenous population and our results cannot be directly generalized to less healthy populations or to countries on different latitudes, with a different socioeconomic status, or with different sleeping habits.

CONCLUSION

We found a modest inverse association of insomnia symptoms with VO_{2peak}, which is the gold standard measure of cardiorespiratory fitness, and the association was independent of

self-reported physical activity. VO_{2peak} is an important determinant of cardiovascular disease,[16] and our findings may therefore be important in the complex interrelation between sleep and the cardiovascular system. Insomnia is a prevalent and manageable condition, and increased focus on adverse health effects of insomnia could be helpful in the prevention of cardiovascular disease. Future studies with a prospective design are needed to confirm our findings and to establish the direction of the relation of insomnia symptoms with cardiorespiratory fitness.

DISCLOSURE STATEMENT

This was not an industry supported study. The authors have indicated no financial conflicts of interest.

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Table S1—Least square means and 95% confidence intervals for the insomnia symptoms and VO_{2peak} (mL/kg/min) when excluding participants reporting sleep disordered breathing and snoring several times per wk

	Model 1[a]		Model 2[b]		Model 3[c]	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
Sleep initiation problems						
Never/almost never	40.0	39.7 – 40.4	40.3	40.0 – 40.6	40.2	39.9 – 40.5
Occasionally	39.9	39.5 – 40.2	40.1	39.8 – 40.4	40.3	40.0 – 40.7
Several times/wk	38.3	37.5 – 39.2	39.1	38.3 – 39.8	39.2	38.4 – 39.9
P value for linear trend	0.002		0.030		0.156	
Repeated awakenings						
Never/almost never	40.4	40.0 – 40.8	40.5	40.2 – 40.9	40.6	402 – 40.9
Occasionally	39.6	39.3 – 40.0	40.0	39.7 – 40.3	40.1	39.8 – 40.4
Several times/wk	38.9	38.4 – 39.5	39.4	38.9 – 40.0	39.5	39.0 – 40.1
P value for linear trend	< 0.001		0.001		0.001	
Early awakening						
Never/almost never	39.8	39.5 – 40.1	40.1	39.8 – 40.4	40.3	40.0 – 40.6
Occasionally	40.0	39.6 – 40.3	40.2	39.8 – 40.5	40.1	39.7 – 40.4
Several times/wk	39.3	38.5 – 40.1	39.9	39.1 – 40.6	39.7	39.0 – 40.5
P value for linear trend	0.593		0.831		0.126	
Daytime sleepiness						
Never/almost never	40.3	39.9 – 40.8	40.4	40.0 – 40.8	40.3	40.0 – 40.7
Occasionally	39.8	39.5 – 40.1	40.1	39.8 – 40.3	40.2	39.9 – 40.4
Several times/week	38.3	37.6 – 39.1	39.4	38.7 – 40.1	39.7	39.0 – 40.4
P value for linear trend	< 0.001		0.031		0.172	

[a]Model 1 is adjusted for age and sex. [b]Model 2 is adjusted for age, sex, marital status, education, smoking, alcohol consumption, systolic and diastolic blood pressure, body mass index, sleep disordered breathing, snoring, serum total cholesterol and high-density lipoprotein cholesterol, depression score, anxiety score, and chronic pain. [c]Model 3 is adjusted for the same variables as in Model 2, and physical activity index and resting heart rate. CI, confidence interval; VO_{2peak}, peak oxygen uptake.

Table S2—Least square means and 95% confidence intervals for the cumulative insomnia symptoms and $VO2_{peak}$ (mL/kg/min) when excluding participants reporting sleep disordered breathing and snoring several times per wk

		Model 1[a]		Model 2[b]		Model 3[c]	
Insomnia symptoms	n	Mean	95% CI	Mean	95% CI	Mean	95% CI
0	2,677	40.0	39.8 – 40.3	40.2	40.0 – 40.5	40.3	40.1 – 40.6
1	408	39.4	38.7 – 40.0	39.7	39.1 – 40.3	40.0	39.4 – 40.6
2	219	38.5	37.6 – 39.4	39.1	38.2 – 39.9	39.1	38.3 – 39.9
3	78	38.7	37.2 – 40.2	39.6	38.2 – 41.1	39.4	38.0 – 40.8
P value for linear trend		< 0.001		0.008		0.004	

[a]Model 1 is adjusted for age and sex. [b]Model 2 is adjusted for age, sex, marital status, education, smoking, alcohol consumption, systolic and diastolic blood pressure, body mass index, sleep disordered breathing, snoring, serum total cholesterol and high-density lipoprotein cholesterol, depression score, anxiety score, and chronic pain. [c]Model 3 is adjusted for the same variables as in Model 2, and physical activity index and resting heart rate. CI, confidence interval; VO_{2peak}, peak oxygen uptake.

Table S3—Least square means and 95% confidence intervals for the insomnia symptoms and VO$_{2peak}$ (mL/kg/min) when excluding participants with diabetes

	Model 1[a]		Model 2[b]		Model 3[c]	
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Sleep initiation problems						
Never/almost never	40.0	39.7 – 40.3	40.4	40.1 – 40.7	40.4	40.1 – 40.6
Occasionally	39.8	39.5 – 40.2	40.1	39.8 – 40.4	40.3	40.0 – 40.7
Several times/wk	38.4	37.6 – 39.1	39.3	38.6 – 40.0	39.4	38.6 – 40.1
P value for linear trend	0.003		0.010		0.099	
Repeated awakenings						
Never/almost never	40.3	40.0 – 40.7	40.6	40.3 – 41.0	40.7	40.3 – 41.0
Occasionally	39.6	39.3 – 39.9	40.0	39.7 – 40.3	40.2	39.9 – 40.5
Several times/wk	38.8	38.3 – 39.4	39.4	38.9 – 39.9	39.5	39.0 – 40.0
P value for linear trend	< 0.001		< 0.001		< 0.001	
Early awakening						
Never/almost never	39.8	39.5 – 40.1	40.2	39.9 – 40.4	40.4	40.1 – 40.7
Occasionally	39.9	39.6 – 40.3	40.1	39.8 – 40.5	40.1	39.8 – 40.4
Several times/wk	39.4	38.6 – 40.2	40.1	39.4 – 40.8	40.0	39.3 – 40.7
P value for linear trend	0.813		0.852		0.207	
Daytime sleepiness						
Never/almost never	40.4	40.0 – 40.8	40.6	40.2 – 40.9	40.5	40.1 – 40.9
Occasionally	39.7	39.5 – 40.0	40.1	39.8 – 40.3	40.2	40.0 – 40.5
Several times/wk	38.1	37.5 – 38.8	39.4	38.7 – 40.0	39.7	39.1 – 40.4
P value for linear trend	< 0.001		0.002		0.044	

[a]Model 1 is adjusted for age and sex. [b]Model 2 is adjusted for age, sex, marital status, education, smoking, alcohol consumption, systolic and diastolic blood pressure, body mass index, sleep disordered breathing, snoring, serum total cholesterol and high-density lipoprotein cholesterol, depression score, anxiety score, and chronic pain. [c]Model 3 is adjusted for the same variables as in Model 2, and physical activity index and resting heart rate. CI, confidence interval; VO$_{2peak}$, peak oxygen uptake.

Table S4—Least square means and 95% confidence intervals for the cumulative insomnia symptoms and VO2$_{peak}$ (mL/kg/min) when excluding participants with diabetes

		Model 1[a]		Model 2[b]		Model 3[c]	
Insomnia symptoms	**n**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
0	3,009	40.0	39.8 – 40.2	40.3	40.1 – 40.5	40.4	40.2 – 40.6
1	482	39.1	38.5 – 39.7	39.7	39.1 – 40.2	39.9	39.3 – 40.4
2	248	38.6	37.7 – 39.4	39.3	38.5 – 40.1	39.3	38.5 – 40.0
3	85	39.0	37.5 – 40.4	40.0	38.6 – 41.3	39.8	38.5 – 41.2
P value for linear trend		< 0.001		0.014		0.004	

[a]Model 1 is adjusted for age and sex. [b]Model 2 is adjusted for age, sex, marital status, education, smoking, alcohol consumption, systolic and diastolic blood pressure, body mass index, sleep disordered breathing, snoring, serum total cholesterol and high-density lipoprotein cholesterol, depression score, anxiety score, and chronic pain. [c]Model 3 is adjusted for the same variables as in Model 2, and physical activity index and resting heart rate.
CI, confidence interval; VO$_{2peak}$, peak oxygen uptake.

Table S5—Least square means and 95% confidence intervals for the insomnia symptoms and VO$_{2peak}$ (mL/kg/min) when excluding participants that did not respond to all the insomnia questions

	Model 1		Model 2		Model 3	
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Sleep initiation problems						
Never/almost never	39.9	39.6 – 40.2	40.3	40.0 – 40.6	40.3	40.0 – 40.6
Occasionally	39.8	39.4 – 40.1	40.0	39.7 – 40.3	40.3	39.9 – 40.6
Several times/wk	38.3	37.5 – 39.1	39.3	38.5 – 40.0	39.3	38.6 – 40.0
P value for linear trend	0.003		0.011		0.083	
Repeated awakenings						
Never/almost never	40.3	40.0 – 40.7	40.6	40.2 – 40.9	40.6	40.3 – 41.0
Occasionally	39.6	39.2 – 39.9	39.9	39.6 – 40.2	40.1	39.8 – 40.4
Several times/wk	38.8	38.3 – 39.4	39.4	38.9 – 39.9	39.5	39.0 – 40.0
P value for linear trend	< 0.001		< 0.001		< 0.001	
Early awakening						
Never/almost never	39.7	39.4 – 40.0	40.1	39.8 – 40.4	40.3	40.1 – 40.6
Occasionally	39.9	39.5 – 40.2	40.1	39.7 – 40.4	40.1	39.8 – 40.4
Several times/wk	39.3	38.6 – 40.1	40.1	39.4 – 40.8	40.0	39.3 – 40.6
P value for linear trend	0.816		0.907		0.183	
Daytime sleepiness						
Never/almost never	40.4	40.0 – 40.8	40.5	40.1 – 40.9	40.5	40.1 – 40.8
Occasionally	39.7	39.4 – 40.0	40.0	39.8 – 40.3	40.2	39.9 – 40.4
Several times/wk	38.1	37.5 – 38.8	39.3	38.7 – 40.0	39.7	39.1 – 40.4
P value for linear trend	< 0.001		0.002		0.044	

CI, confidence interval; VO$_{2peak,}$ peak oxygen uptake.