Habitual sleep measures are associated with overall body fat, and not specifically with visceral fat in men and women

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Study design: SAD, RN, DvH, RdM. **Data analyses**: SAD, RN. **Data acquisition**: NRB, HJL, AdR, FRR, RdM. **Overall study design and management**: FRR, RdM. **Interpretation of the data:** SAD, RN, NRB, PCNR, DvH, RdM. **Drafting the manuscript:** SAD, RN. **Commenting on the initial versions of the manuscript and final approval for submission**: SAD, RN, NRB, AdR, HJL, FRR, PCNR, DvH, RdM.

What is already known about this subject?

- Short sleep duration and poor sleep quality are associated with increased body fat.
- Body mass index and waist circumference are poor measures of fat deposition in different compartments.

What does this study add?

- Short sleep duration and poor sleep quality are associated with a higher amount of visceral adipose tissue in men and women, but this association disappeared after adjustment for total body fat.
- Short sleep duration and poor sleep quality are not specifically associated with a higher amount of visceral adipose tissue.

Abstract

Objective: To investigate the associations of sleep duration and sleep quality with visceral adipose tissue (VAT) in middle-aged individuals.

Methods: In this cross-sectional analysis of baseline measurements of the Netherlands Epidemiology of Obesity study, participants underwent anthropometry and completed the Pittsburgh Sleep Quality Index (PSQI) for assessing short sleep duration (as sex-specific age-adjusted percentiles) and poor quality (PSQI>5). VAT was assessed by magnetic resonance imaging in a random subgroup. We performed linear regression analyses to examine associations of short sleep and poor sleep with measures of body fat, adjusted for confounding including total body fat in models with VAT.

Results: A total of 5,094 participants (52% women; mean [SD] age of 56 [6] years), of whom 1,947 with VAT, were analyzed. The difference in VAT between poor sleep (PSQI>5) compared to good sleep (PSQI≤5) was 7.2 (95%CI:1.2, 13.8) cm^2 in women and 16.1 (95%CI:6.2, 26.0) cm^2) in men. These differences attenuated toward the null after the adjustment for total body fat. Similar patterns of associations were observed for short sleep (lowest 10% as compared to median 60%).

Conclusions: Our results suggest that measures of sleep are not specifically associated with a higher amount of VAT.

Introduction

Obesity, in particular abdominal obesity, is a well-established risk factor for metabolic and cardiovascular diseases (1). Multiple factors have thus far been identified to contribute to the risk of obesity. In addition to well-known determinants for obesity as a sedentary lifestyle and high caloric intake, broad consensus has been reached in just a few years that short total sleep time and poor sleep quality are associated with a higher body mass index (BMI) (2, 3, 4, 5, 6, 7, 8, 9, 10). In addition, some of these studies observed an association between long total sleep time and BMI as well, which suggests that there could be a U-shaped relation between total sleep time and BMI (3, 6). The hypothesis of a short habitual sleep duration leading to higher body fat is supported by intervention studies. For example, sleep curtailment causes a change in circulating ghrelin and leptin concentrations, hormones essential for sensing hunger and satiety (11, 12). Even one night of sleep curtailment causes leptin levels and feeling of satiety to decrease, and ghrelin levels to increase, subsequently increasing the feeling of hunger.

Abdominal adiposity is characterized by storage of excess fat in the abdominal subcutaneous and visceral adipose tissue (VAT). In particular, VAT has been shown to be a strong risk factor for diseases like type 2 diabetes mellitus and cardiovascular diseases (5, 13, 14, 15, 16). Because direct assessment of VAT by magnetic resonance imaging is not widely available in large cohort studies, studies often investigated the association between sleep duration and waist circumference, as a measure of abdominal adiposity and a proxy of VAT (3, 4, 5, 17). These studies observed that short sleep duration, and not long sleep duration, was associated with a larger waist circumference. The association between poor sleep quality and waist circumference is less well studied, but available literature suggests that poor sleep quality is associated with a higher waist circumference (18, 19).

Waist circumference, however, does not distinguish abdominal subcutaneous fat from visceral fat. Given that VAT is a strong risk factor for insulin resistance (5, 13, 14, 15, 16), and different measures of habitual sleep have been associated with insulin resistance and type 2 diabetes mellitus (20, 21, 22), we hypothesized that short sleep duration as well as poor sleep quality are specifically associated with a higher amount of VAT. Therefore, the aim of this study was to investigate the associations of sleep duration and sleep quality with VAT in a population-based study comprising Dutch middle-aged men and women.

Methods

Study design and study population

The present study is a cross-sectional analysis of baseline measurements of the Netherlands Epidemiology of Obesity (NEO) study, a population-based, prospective cohort study. The NEO study started in 2008 and included 6,671 individuals aged 45–65 years, with an oversampling of individuals with overweight or obesity. The study design and population is described in detail elsewhere (23). Men and women living in the greater area of Leiden (in the West of the Netherlands) were invited to participate if they were aged between 45 and 65 years and had a self-reported BMI of 27 kg/m^2 or higher. In addition, all inhabitants aged between 45 and 65 years from one municipality (Leiderdorp) were invited to participate irrespective of their BMI, allowing for a reference group with a normal BMI distribution. The Medical Ethical Committee of the Leiden University Medical Center (LUMC) approved the design of the study. All participants gave their written informed consent.

Participants were invited for a baseline visit at the NEO study centre of the LUMC. Prior to the study visit, participants completed a general questionnaire at home to report demographic, lifestyle and clinical information. Collection of data from the Pittsburgh sleep quality index (PSQI) questionnaire only started as from July 2009. For this reason, participants (N = 1,402) included before July 2009 without PSQI data were not included in the present study. The participants were asked to bring all medication they were using to the study visit for a medication inventory.

At the study site, a screening form was completed by all participants asking about anything that might create a health risk or interfere with MRI imaging (most notably metallic devices, claustrophobia, and a body circumference of more than 1.70 m). Of the participants who were eligible for MRI, approximately 35% of the total study population were randomly selected to undergo direct assessment of VAT.

Of the participants with PSQI data, participants with missing data on either waist circumference or total body fat (TBF) (n=30) or covariates (n=145) were excluded from the analyses. For the analyses on VAT, only participants with a measurement of VAT were included (n=1,947).

Assessment of sleep quality and duration

To assess sleep duration, we made use of the question related to this topic on the Pittsburgh sleep quality index (PSQI) questionnaire: "During the past month, how many hours of actual sleep did you get at night. To facilitate the interpretation of the observations whether there is a non-linear (e.g., U-shape) relationship between sleep duration and measures of adiposity, we studied the associations between sleep duration and measures of adiposity in different strata based on sleep duration. Because there is no consensus in the literature to define short and long total sleep time (2, 3, 4, 5, 6, 7, 8, 9, 10, 17), and defining groups of participants based on the sleep duration could be misclassified because of age and sex, we standardized sleep durations based on the residuals, adjusted for age and stratified by sex. Based on percentiles of these residuals, we defined the shortest sleepers (0-10 percentile), short sleepers (10-20 percentile), middle sleepers (20-80 percentile, reference group), long sleepers (80-90 percentile) and the longest sleepers (90-100 percentile).

Sleep quality was based on the total PSQI score, which ranges from 0 to 21. A score of ≤5 is considered good sleep quality, whereas a score of >5 is considered poor sleep quality (24). In addition, we defined participants with a PSQI score of ≥8 as worse sleep quality.

Measures of body fat

Body weight and percent body fat were measured by the Tanita bio impedance balance (TBF-310, Tanita International Division, UK) without shoes and one kilogram was subtracted to correct for the weight of clothing. Height was measured without shoes with a vertically fixed, calibrated tape measure. BMI was calculated by dividing the weight in kilograms by the height in meters squared. Waist circumference was measured with a horizontally placed tape measure mid-way between the lower costal margin and the iliac crest with a precision of 0.1 cm.

Abdominal subcutaneous and visceral fat were quantified by a turbo spin echo imaging protocol using MRI in 1,947 participants with exposure and covariate data. Imaging was performed on a 1.5 Tesla MR system (Philips Medical Systems, Best, the Netherlands). The VAT depots was quantified by converting the number of pixels to square cm for all three slides using in-house-developed software (MASS, Medis, Leiden, the Netherlands). At the level of the 5th lumbar vertebra three transverse images each with a slice thickness of 10 mm were obtained during a breath-hold. The mean of VAT from the three slices was calculated and used in the analyses.

Covariates

Based on questionnaires, participants reported ethnicity by self-identification in eight categories which we grouped into white and other. Tobacco smoking was reported in the three categories: current smoker, former smoker, or never smoker. Highest level of education was reported in 10 categories according to the Dutch education system and participants with none, primary school or lower vocational education were categorized as lower educated and the others as higher educated. Alcohol and coffee consumption were self-reported on a food frequency questionnaire. Alcohol consumption was expressed in grams of alcohol per day and coffee consumption as cups per day. Participants reported the frequency, duration and intensity of their usual physical activity during leisure times using the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH) (25, 26). For this questionnaire, participants reported the frequency and duration of their physical activity during leisure time and this was expressed in hours per week of metabolic equivalents. Menopausal status was divided into three categories (pre-, peri-, and postmenopausal) based on information on oopho- or hysterectomy and/or self-reported menopausal status. Women who reported a hysterectomy were classified according to their age (premenopausal when <46 years, peri-menopausal when 46 to 55 years, and postmenopausal when ≥55 years). Women who did not report menopausal status and were 58 years or older were classified as postmenopausal. Use of hormones (hormone replacement therapy and oral contraceptives) and of sleep medication was based on a medication inventory.

Statistical analysis

In the NEO study, persons with a BMI of 27 kg/m^2 or higher are oversampled. To correctly represent associations for the general population (27), adjustments for the oversampling of participants with a BMI ≥ 27 kg/m^2 are made. This is done by weighting individuals towards the BMI distribution of participants from the Leiderdorp municipality (28), whose BMI distribution was similar to the BMI distribution of the general Dutch population (29). All results are based on weighted analyses. Consequently, the results apply to a population-based study without oversampling of individuals with a BMI ≥27 kg/m^2. All analyses are performed using STATA version 12.1 (StataCorp LP, TX, US).

Baseline characteristics of the study population were expressed as mean (with standard deviation [SD]), median (inter quartile range [IQR]) or proportion (%), in the whole study population and separately for men and women (**Table 1**). Given the known differences in body fat distribution and habitual sleep between men and women, all analyses were performed separately for men and women. In the first analyses, we aimed to confirm well-established associations between short habitual sleep duration and poor sleep quality and

BMI, waist circumference and total body fat in the total study population (2, 3, 4, 5, 6, 7, 8, 9, 10). Subsequently, we repeated these analyses for the subpopulation of participants who underwent MRI, and investigated the association between short habitual duration and poor sleep quality and VAT. To examine the associations between sleep duration and the measures of adiposity, we performed multivariable linear regression analyses. We calculated the mean difference in adiposity measure in the sleep duration groups and sleep quality groups compared with the reference groups (20-80% middle sleep duration and PSQI≤5) with corresponding 95% confidence intervals. We adjusted crude models for age, physical activity, menopausal state, ethnicity, alcohol consumption, coffee consumption, smoking, education and the use of oral contraceptives and hormone replacement therapy (ATC-code: G03A, G03C, G03F). The models of sleep duration were additionally adjusted for sleep medication (ATC-code: N05C) use. We additionally performed joint models and adjusted the analyses of sleep duration for sleep quality and vice versa to provide insights on the relative contributions of these two measures of habitual sleep to the measures of adiposity. We adjusted the analyses concerning VAT for TBF to investigate to what extent associations were specific for VAT instead of merely a reflection of associations with overall adiposity. Finally, we tested whether the associations between habitual sleep and measures of adiposity were different between men and women by including an interaction term between sex and the measure of habitual sleep in the fully adjusted models.

Results

Characteristics of the study population

A total of 5,094 participants completed the PSQI-questionnaire and had complete data on potential confounding factors. Of these, VAT was assessed in 1,947 participants. In the total study population (54% women) (**Table 1**), mean (SD) age was 55.7 (6.0) years.

Mean (SD) sleep duration was 7.1 (1.0) hours in women and 6.9 (1.0) hours in men. PSQI score had a median (IQR) of 5 (3, 7) in women and 4 (2, 5) in men. Whereas women had more total body fat than men, men had a larger waist circumference and more VAT than women. The characteristics of the subpopulation with VAT assessment were similar to the total study population (**Supplement Table 1**).

Associations between sleep duration and measures of adiposity

Compared with the reference population (**Table 2**), we observed that both in men and women the group of the shortest sleepers had a higher BMI (mean difference [95% confidence interval] in women 1.9 [1.0, 2.9] kg/m^2; in men 1.3 [0.6, 2.0] kg/m^2), larger waist circumference (women 4.2 [1.6, 6.8] cm, men 3.9 [1.9, 6.0] cm) and more TBF (women 2.3 [0.9, 3.6] %, men 1.7 [0.6, 2.9] %). These results did not materially differ when we adjusted for potential confounding factors. Additional adjustment for sleep quality only slightly attenuated the associations (results not shown). Compared with the reference population, short, long and longest sleep were not associated with BMI, waist circumference or TBF. We observed similar associations for BMI, waist circumference and TBF in the subpopulation of participants who underwent MRI (**Supplementary Table 2**).

Compared with the reference group (**Figure 1**), the shortest sleep group had more VAT (women 16.4 [3.1, 29.8] cm^2, men 10.2 [-4.1, 24.2] cm^2). However, additional adjustment of the associations for TBF, attenuated the estimates for shortest sleep duration towards the null (women 6.4 [-1.4, 14.1] cm^2, men 0.6 [-10.8, 12.0] cm^2). No evidence was observed for differences between men and women (P-value for interaction > 0.05).

Associations between sleep quality and measures of adiposity

Table 3 shows the mean differences in BMI, waist circumference and TBF associated with the sleep quality groups (poor sleep quality PSQI >5; worse sleep quality PSQI ≥8) compared with the reference group (PSQI≤5). In crude models, poor sleep quality was associated with higher BMI (women 0.8 [0.4, 1.2] kg/m^2, men 0.7 [0.3, 1.2] kg/m^2), larger waist circumference (women 1.8 [0.6, 3.1] cm, men 2.5 [1.2, 3.8] cm) and more TBF (women 1.1 [0.4, 1.8] %, men 1.1 [0.4, 1.8] %). In line, worse sleep quality (PSQI ≥8) was associated with higher BMI (women 1.1 [0.6, 1.6] kg/m^2, men 0.8 [0.1, 1.4] kg/m^2), larger waist circumference (women 2.7 [1.1, 4.2] cm, men 2.6 [0.7, 4.4] cm) and more TBF (women 1.7 [0.8, 2.5]% , men 1.3 [0.3, 2.3] %). These associations attenuated after adjustment for potential confounding factors. Additional adjustment for sleep duration did not notably change the associations (results not shown). We observed similar associations for BMI, waist circumference and TBF in the subpopulation of participants who underwent MRI (**Supplementary Table 3**).

Compared with normal sleep (PSQI ≤5), poor sleep quality was associated with more VAT in men (17.5 cm^2 [7.2, 27.8]) and women (7.5 cm^2 [1.2, 13.8]); estimates did not materially change after adjustment for potential confounding factors with the exception of TBF (**Figure 2**). Associations of worse sleep were in similar direction as compared with normal sleep, although with larger confidence intervals (women 9.3 cm^2 [1.2, 17.4]; men 9.1 cm^2 [-3.5, 21.8]). After additional adjustment for TBF the associations attenuated toward the null (poor quality: women -1.4 [-5.9, 3.1] cm^2, men 6.5 [-1.6, 14.5] cm^2; worse quality:

women -2.2 [-7.9, 3.5] cm^2, men 2.3 [-6.7, 11.2] cm^2) (**Figure 2**). No evidence was observed for differences between men and women (P-value for interaction > 0.05).

Discussion

In the present population-based study of middle-aged men and women, we observed that short sleep duration and poor sleep quality were associated with measures of overall and abdominal adiposity, but we did not observe a clear dose-response relationship between sleep quality and abdominal adiposity. However, associations of sleep quality and duration with visceral fat disappeared after adjustment for TBF. These results suggest that, although measures of sleep were associated with TBF and other measures of overall adiposity, short habitual sleep duration and quality were not specifically associated with VAT. These results were similarly observed for men and women.

The observed associations with BMI, waist circumference and TBF are consistent with other observational studies, showing that short sleep duration and poor sleep quality are associated with having more body fat (2, 3, 4, 5, 6, 7, 8, 9, 10). Besides the observation that men and women have different sleeping habits (women tend to sleep longer, and have a higher risk of experiencing insomnia during their lifespan, and 33-51% of women report sleep complaints during menopausal transition (30)), and have a different body fat distribution, the observed associations of sleep duration and sleep quality with adiposity were similar in men and women. The observation that the association of short sleep duration and poor sleep quality with VAT attenuated after adjustment for TBF, is in line with a cross-sectional study performed in a Japanese population (31). In 5,400 Japanese men with self-reported sleep data, and computed tomography data to determine body fat depots, short sleep duration was associated with higher BMI, waist circumference, abdominal subcutaneous adipose tissue and VAT. However, when the association with VAT was adjusted for abdominal subcutaneous adipose tissue, this association disappeared, which is consistent with our findings. While we observed an association between short sleep duration and adiposity in both men and women, there was no association in Japanese women, although this discrepance in results could also be due to a limited sample size (n=642) (31).

Our results suggest that a habitual short sleep duration and poor sleep quality are associated with general adiposity rather than abdominal adiposity. A possible reason for the lack of an association between sleep and VAT independent of total body fat could be either explained by a too low number of individuals classified as short sleeper or that the association between sleep measures and VAT does not exist independent of overall adiposity. Furthermore, the group classified as short sleepers reported a sleep duration ranging between 1.7 and 5.7 hours. However, as there is no consensus about the definition of short sleep (2, 3, 4, 5, 6, 7, 8, 9, 10, 17), we are not able to determine whether the total sleep duration in this group is sufficiently short to observe any associations. Unlike some of the previous studies (3, 6), we did not observe a U-shape between sleep duration and adiposity in this population. One potential explanation could be that sleep was not sufficiently long in the percentiles which we defined as long sleep (sleep duration in the upper percentile ranged between 8 and 13 hours). Although we classified the highest percentile as long sleep duration; the sleep duration reported by this group still only ranged between 8.0 and 13.0 hours. As there is no consensus about the definition of long sleep (2, 3, 4, 5, 6, 7, 8, 9, 10, 17), it is unclear whether this group includes a sufficient number of long sleepers. Also, the majority of the other studies did not observe a U-shape (2, 4, 5, 7, 8, 9, 10). Therefore, it is possible that the few (smaller) studies that observed this U-shape found a false-positive association between long sleep and increased adiposity.

One of the strengths of our study is the direct assessment of visceral fat with MRI (32) in a relatively large study population. A limitation of this study is its cross-sectional and observational design. As a result, we cannot draw conclusions on the direction and causality of the associations between measures of sleep and adiposity. In literature, evidence for both directions is described. It has been shown that even one night of sleep deprivation can lead to decreased leptin levels, and increased ghrelin levels, which subsequently increase appetite (11, 12). Furthermore, a recent genome-wide association study on different measures of habitual sleep found a shared genetic component of insomnia symptoms and obesity risk (33). However, obesity has also been described as an important risk factor for multiple sleeping disorders, which includes sleep apnea (34, 35). Another limitation is that sleep data was self-reported, and objective sleep measurements with actigraphy or polysomnography may be more reliable methods to assess sleep duration and quality. Other studies have investigated the association between objective sleep measures and adiposity. For example, Moraes *et al.*(4) used both actigraphy and polysomnography to assess sleep duration. Also they observed an association between short sleep duration, measured by both actigraphy and polysomnography, and increased adiposity. And last, this study was done in a study population predominantly of European ancestry. For this reason, our results need to be confirmed in populations of different ancestry backgrounds. However, in the Multi-Ethnic Study of Atherosclerosis (MESA) study short sleep duration (<6 hours) was associated with higher BMI, waist circumference and TBF, also after adjustment for race, and there was no evidence for effect modification by race (10).

Taken together, both short sleep duration and poor sleep quality are associated with more overall body fat in middle-aged men and women and these associations were not specific for VAT. The previously observed associations between disturbances in measures of habitual sleep (e.g., short sleep duration, poor sleep quality) and insulin resistance and type 2 diabetes mellitus (20, 21, 22) is therefore not likely to be specifically affected by higher amounts of VAT in individuals with short sleep duration and poor sleep quality. Future prospective studies should investigate the direction of the associations between sleep duration and quality with overall body fat in longitudinal studies.

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FIGURE LEGENDS

Figure 1: Associations between sleep duration and VAT in 1947 participants in the NEO study aged between 45 and 65 years.

Results were based on analyses weighted towards the BMI distribution of the general population (n=1947; 1032 men, 915 women). Results van be interpreted as the mean difference (with 95% confidence interval) in VAT (in cm^2) between the index and reference group. Model 1, crude model. Model 2, adjusted for age, physical activity, education, ethnicity, alcohol consumption, coffee consumption, and smoking. Model 3, Model 2 + total body fat. Models 2 and 3 in women were additionally adjusted for menopausal status and the use of hormones.

Figure 2: Associations between sleep quality and VAT in 1947 participants in the NEO study aged between 45 and 65 years.

Results were based on analyses weighted towards the BMI distribution of the general population (n=1947; 1032 men, 915 women). Results van be interpreted as the mean difference (with 95% confidence interval) in VAT (in cm^2) between the index and reference group. Model 1, unadjusted for potential confounding factors. Model 2, adjusted for age, physical activity, education, ethnicity, alcohol consumption, coffee consumption, and smoking. Model 3, Model 2 + total body fat. Models 2 and 3 in women were additionally adjusted for menopausal status and the use of hormones.

Table 1: Characteristics of the participants in the Netherlands Epidemiology of Obesity study, and stratified by sex.

Characteristics	Total population	Women (56%)	Men (44%)
Age (years), mean (SD)	56 (6)	55.5 (6)	56 (6)
BMI (kg/m^2), mean (SD)	26.0 (4)	25.6 (5)	27 (4)
Total body fat (%),mean (SD)	31 (9)	36.4 (7)	25 (6)
Waist circumference (cm), mean (SD)	91 (13)	86 (13)	98 (11)
VAT (cm^2) (n=1947), median (SD)	76 (47, 116)	54 (36, 84)	101 (73, 140)
Total sleep duration (hours/night), mean (SD)	7 (1)	7 (1)	7 (1)
Pittsburgh score, median (IQR)	4 (3, 6)	5 (3, 7)	4 (2, 5)
Education (high [a]), %	47 ± 1.4	45 ± 1.9	49 ± 2.0
Ethnicity (white), %	95 ± 0.6	95 ± 0.8	95 ± 0.9
Alcohol consumption (grams/day), median (IQR)	10 (3, 21)	8 (2, 15)	17 (6, 28)
Physical activity (MET-hours/week), median (IQR)	30 (16, 50)	30 (17, 49)	31 (16, 51)
Coffee consumption [b], %			
0 cups/day	5 ± 0.6	7 ± 1.0	2 ± 0.6
>0-4 cups/day	61 ± 1.3	68 ± 1.8	52 ± 2.0
>4 cups/day	34 ± 1.3	25 ± 1.7	46 ± 2.0
Smoking, %			
Current	16 ± 1.0	15 ± 1.4	18 ± 1.5
Former	45 ± 1.4	44 ± 1.9	46 ± 2.0
Use of hypnotics and sedatives, %	4 ± 0.5	5 ± 0.8	2 ± 0.6
Hormone use [c], %			
Current		10 ± 1.1	-
Former		81 ± 1.5	-
Post-menopausal state, %		60 ± 1.9	-

Results were based on analyses weighted towards the BMI distribution of the general population (n=5094; 2449 men and 2645 women). Data are shown as mean (SD), median (IQR) or percentage ± 95% confidence interval for measurement dispersion.
BMI: Body Mass Index; NEO: Netherlands Epidemiology of Obesity; VAT: visceral adipose tissue; MET: metabolic equivalent.
[a] High education: higher general secondary education, pre-university education, higher vocational education, university.
[b] Coffee cup defined as 125 ml/cup.

[c] Hormone use: use of sex hormones, as taken by oral contraceptives or hormone replacement therapy.

Table 2: Associations between sleep duration and BMI, WC and TBF in 5094 participants in the NEO study aged between 45 and 65 years

	Shortest sleep (0-10%) Men = 1.7-5.7 hrs Women = 2.5-5.4 hrs	Short sleep (10-20%) Men = 5.7-6.0 hrs Women = 5.4-5.9 hrs	Reference (20-80%) Men = 6.0-7.7 hrs Women = 5.9-7.9 hrs	Long sleep (80-90%) Men = 7.7-8.0 hrs Women = 7.9-8.0 hrs	Longest sleep (90-100%) Men = 8.0-13.0 hrs Women = 8.0-12.9 hrs
Body mass index (kg/m^2)					
Men, model 1	1.3 (0.6, 2.0)	-0.1 (-0.7, 0.6)	-	0.2 (-0.5, 0.8)	-0.2 (-0.8, 0.6)
Men, model 2	1.2 (0.5, 1.8)	-0.1 (-0.7, 0.5)	-	0.2 (-0.4, 0.9)	-0.4 (-1.1, 0.3)
Women, model 1	1.9 (1.0, 2.9)	0.5 (-0.3, 1.3)	-	0.2 (-0.5, 0.9)	0.2 (-0.5, 1.1)
Women, model 2	1.6 (0.7, 2.6)	0.4 (-0.4, 1.2)	-	0.1 (-0.7, 0.8)	0.2 (-0.6, 1.0)
Waist circumference (cm)					
Men, model 1	3.9 (1.9, 6.0)	-0.2 (-2.2, 1.7)	-	0.4 (-1.6, 2.4)	0.0 (-2.1, 2.1)
Men, model 2	3.4 (1.5, 5.4)	-0.5 (-2.5, 1.4)	-	0.7 (-1.2, 2.5)	-0.6 (-2.6, 1.4)
Women, model 1	4.2 (1.6, 6.8)	1.8 (-0.3, 4.0)	-	0.1 (-1.8, 2.1)	1.4 (-0.8, 3.6)
Women, model 2	3.6 (1.0, 6.2)	1.3 (-1.0, 3.5)	-	0.1 (-1.9, 2.1)	1.4 (-0.8, 3.6)
Total body fat (%)					
Men, model 1	1.7 (0.6, 2.9)	0.0 (-1.0, 1.1)	-	-0.1 (-1.2, 1.1)	-0.1 (-1.2, 1.1)
Men, model 2	1.4 (0.3, 2.5)	-0.2 (-1.3, 0.8)	-	-0.1 (-1.2, 0.9)	-0.5 (-1.6, 0.7)
Women, model 1	2.3 (0.9, 3.6)	0.8 (-0.6, 2.2)	-	-0.2 (-1.4, 1.0)	0.6 (-0.8, 1.9)
Women, model 2	1.9 (0.6, 3.3)	0.5 (-0.9, 1.8)	-	-0.2 (-1.5, 1.1)	0.5 (-0.9, 1.9)

Results are presented as the mean differences (with 95% confidence interval) compared with the reference group, and based on analyses weighted towards the BMI distribution of the general population (n=5094; 2449 men and 2645 women). Model 1, crude model. Model 2, adjusted for age, physical activity, education, ethnicity, use of hypnotics and sedatives, alcohol consumption, coffee consumption and smoking. Analyses in women were additionally adjusted for menopausal status and use of hormones.

Table 3: Associations between sleep quality and BMI, WC and TBF in 5094 participants in the NEO study aged between 45 and 65 years.

	Reference (PSQI ≤5)	Poor sleep quality (PSQI >5)	Worse sleep quality PSQI ≥8
Body mass index (kg/m²)			
Men, model 1	-	0.7 (0.3, 1.2)	0.8 (0.1, 1.4)
Men, model 2	-	0.7 (0.2, 1.1)	0.7 (0.1, 1.3)
Women, model 1	-	0.8 (0.4, 1.2)	1.1 (0.6, 1.6)
Women, model 2	-	0.6 (0.1, 1.0)	0.8 (0.3, 1.3)
Waist circumference (cm)			
Men, model 1	-	2.5 (1.2, 3.8)	2.6 (0.7, 4.4)
Men, model 2	-	2.3 (1.1, 3.6)	2.5 (0.7, 4.3)
Women, model 1	-	1.8 (0.6, 3.1)	2.7 (1.1, 4.2)
Women, model 2	-	1.2 (-0.0, 2.4)	1.9 (0.4, 3.4)
Total body fat (%)			
Men, model 1	-	1.1 (0.4, 1.8)	1.3 (0.3, 2.3)
Men, model 2	-	1.0 (0.3, 1.8)	1.2 (0.3, 2.2)
Women, model 1	-	1.1 (0.4, 1.8)	1.7 (0.8, 2.5)
Women, model 2	-	0.8 (0.1, 1.5)	1.2 (0.4, 2.1)

Results are presented as the mean differences (with 95% confidence interval) compared with the reference group, and based on analyses weighted towards the BMI distribution of the general population (n=5094; 2449 men and 2645 women). Model 1, crude model. Model 2, adjusted for age, physical activity, education, ethnicity, alcohol consumption, coffee consumption and smoking. Women are additionally adjusted for menopausal status and use of hormones. Reference group, 61.2% women, 76.4% men; PSQI>5, 38.9% women, 23.6% men; PSQI≥8, 21.7% women, 11.2% men.

Supplement Table 1: Characteristics of 1,947 participants who underwent MRI and completed the PSQI questionnaire in the NEO study, and stratified by sex.

Characteristics	Total population	Women (53%)	Men (47%)
Age (years)	56 (6)	55 (6)	55.9 (6)
BMI (kg/m^2)	26 (4)	25 (4)	26.4 (3)
Total body fat (%)	30 (8)	35.7 (6)	24.3 (5)
Waist circumference (cm)	90 (12)	84 (12)	97 (10)
VAT (cm^2)	76 (47, 116)	54 (36, 84)	101.4 (73, 140)
Total sleep-duration (hours/night)	7 (1)	7 (1)	7 (1)
Pittsburgh score	4 (3, 6)	5 (3, 7)	4 (2, 5)
Education (% high [a])	47 ± 1.1	43 ± 1.6	51 ± 1.6
Ethnicity (% white)	96 ± 0.4	95 ± 0.7	96 ± 0.6
Alcohol consumption (g/day)	10 (3, 21)	8 (2, 15)	17 (5, 28)
Physical activity (MET-hours/week)	31 (16, 52)	30 (16, 51)	32 (16, 54)
Coffee consumption [b]			
- 0 cups/day	5 ± 0.5	7 ± 0.8	2 ± 0.4
- >0-4 cups/day	59 ± 1.1	66 ± 1.6	51 ± 1.6
- >4 cups/day	37 ± 1.1	27 ± 1.5	47 ± 1.6
Smoking			
- Current	14 ± 0.8	13 ± 1.1	15 ± 1.1
- Former	46 ± 1.3	45 ± 1.6	46 ± 1.6
Use of hypnotics and sedatives	3 ± 0.4	4 ± 0.6	2 ± 0.4
Hormone use [c]			
- Current	-	9 ± 0.9	-
- Former	-	82 ± 1.3	-
Post-menopausal state (%)	-	58 ± 1.6	-

Results were based on analyses weighted towards the BMI distribution of the general population (n=1947; 1032 men, 915 women). Data are shown as mean (SD), median (IQR) or percentage ± 95% confidence interval for measurement dispersion.

BMI: Body Mass Index; MET: metabolic equivalent; NEO: Netherlands Epidemiology of Obesity; VAT: visceral adipose tissue; SAT: abdominal subcutaneous adipose tissue.

[a] High education: High education: higher general secondary education, pre-university education, higher vocational education, university.

[b] Coffee cup defined as 125 ml/cup.

[c] Hormone use: use of sex hormones, either oral contraceptives or hormone replacement therapy

Supplementary Table 2: Associations between sleep duration and BMI, WC and TBF in 1,947 participants in the NEO study aged between 45 and 65 years. The study population is grouped according to sleep duration

	Shortest sleep (0-10%) Men = 1.7-5.7 hrs Women = 2.9-5.4 hrs	Short sleep (10-20%) Men = 5.7-6.0 hrs Women = 5.4-5.9 hrs	Reference (20-80%) Men = 6.0-7.7 hrs Women = 5.9-7.9 hrs	Long sleep (80-90%) Men = 7.7-8.0 hrs Women = 7.9-8.0 hrs	Longest sleep (90-100%) Men = 8.0-10.8 hrs Women = 8.0-10.9 hrs
Body mass index (kg/m^2)					
Men, model 1	1.2 (0.3, 2.1)	-0.6 (-1.5, 0.4)	-	-0.1 (-0.9, 0.8)	-0.6 (-1.6, 0.3)
Men, model 2	1.2 (0.2, 2.1)	-0.7 (-1.6, 0.3)	-	-0.0 (-0.8, 0.8)	-0.9 (-1.8, 0.1)
Women, model 1	1.7 (-0.3, 3.1)	0.5 (-0.8, 1.7)	-	-0.4 (-1.4, 0.5)	0.4 (-0.8, 1.6)
Women, model 2	1.4 (-0.2, 2.7)	0.3 (-0.9, 1.4)	-	-0.4 (-1.3, 0.5)	0.1 (-1.1, 1.4)
Waist circumference (cm)					
Men, model 1	4.7 (2.2, 7.2)	-0.2 (-2.8, 2.3)	-	0.4 (-2.5, 3.3)	-1.0 (-3.8, 1.7)
Men, model 2	4.4 (2.0, 6.9)	-1.0 (-3.6, 1.6)	-	0.3 (-2.4, 3.0)	-1.9 (-4.7, 0.9)
Women, model 1	3.4 (-0.7, 7.6)	2.4 (-0.6, 5.4)	-	0.0 (-2.9, 2.9)	1.3 (-1.9, 4.5)
Women, model 2	2.5 (-1.4, 6.5)	1.4 (-1.6, 4.4)	-	0.0 (-2.9, 3.0)	0.8 (-2.6, 4.3)
Total body fat (%)					
Men, model 1	1.3 (-0.1, 2.8)	-0.3 (-1.7, 1.1)	-	-0.0 (-1.5, 1.5)	-1.2 (-2.8, 0.3)
Men, model 2	1.3 (-0.1, 2.7)	-0.8 (-2.3, 0.6)	-	-0.1 (-1.4, 1.2)	-1.6 (-3.2, -0.0)
Women, model 1	1.6 (-0.8, 4.0)	0.4 (-1.5, 2.3)	-	-0.3 (-2.2, 1.7)	-0.1 (-2.1, 1.9)
Women, model 2	1.2 (-1.0, 3.4)	-0.0 (-1.8, 1.8)	-	-0.4 (-2.4, 1.6)	-0.4 (-2.5, 1.7)

Results were based on analyses weighted towards the BMI distribution of the general population (n=1947; 1032 men, 915 women) and are presented as the mean differences (with 95% confidence interval) compared with the reference group. Model 1, crude. Model 2, adjusted for age, physical activity, education, ethnicity, use of hypnotics and sedatives, alcohol consumption, coffee consumption and smoking. Models in women were additionally adjusted for menopausal status and use of hormones.

Supplementary Table 3: Associations between sleep-quality and BMI, WC and TBF in 1,947 participants in the NEO study aged between 45 and 65 years. The study population is grouped according to PSQI score.

	Reference (PSQI ≤5)	Poor sleep quality (PSQI >5)	Worse sleep quality PSQI ≥8
Body mass index (kg/m²)			
Men, model 1	-	1.1 (0.5, 1.6)	0.8 (0.0, 1.6)
Men, model 2	-	1.0 (0.4, 1.6)	0.8 (0.1, 1.6)
Women, model 1	-	1.3 (0.7, 1.9)	1.5 (0.7, 2.3)
Women, model 2	-	1.2 (0.6, 1.8)	1.5 (0.7, 2.2)
Waist circumference (cm)			
Men, model 1	-	3.5 (1.7, 5.3)	2.2 (-0.1, 4.6)
Men, model 2	-	3.4 (1.6, 5.1)	2.2 (-0.2, 4.6)
Women, model 1	-	3.1 (1.2, 5.0)	3.8 (1.4, 6.2)
Women, model 2	-	2.6 (0.7, 4.4)	3.2 (0.9, 5.6)
Total body fat (%)			
Men, model 1	-	1.5 (0.5, 2.5)	1.0 (-0.3, 2.3)
Men, model 2	-	1.5 (0.5, 2.5)	1.1 (-0.2, 2.4)
Women, model 1	-	1.7 (0.5, 2.8)	2.1 (0.6, 3.6)
Women, model 2	-	1.4 (0.3, 2.5)	1.9 (0.4, 3.3)

Results were based on analyses weighted towards the BMI distribution of the general population (n=1947; 1032 men, 915 women). Results are presented as the mean differences (with 95% confidence interval) compared to the reference group. Model 1, crude. Model 2, adjusted for age, physical activity, education, ethnicity, alcohol consumption, coffee consumption and smoking. Models in women were additionally adjusted for menopausal status and use of hormones. Reference group, 65.5% women, 77.5% men; PSQI>5, 34.5% women, 22.5% men; PSQI≥8, 19.8% women, 10.9% men.