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Title	Serum 25-hydroxyvitamin D-3 levels and poor sleep quality in a Japanese population : the DOSANCO Health Study
Author(s)	Nakamura, Koshi; Hui, Shu-Ping; Ukawa, Shigekazu et al.
Citation	Sleep Medicine, 57, 135-140 https://doi.org/10.1016/j.sleep.2019.01.046
Issue Date	2019-05
Doc URL	https://hdl.handle.net/2115/77808
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Rights(URL)	https://creativecommons.org/licenses/by-nc-nd/4.0/
Type	journal article
File Information	Nakamura K_Manuscript (Sleep Med).pdf

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Serum 25-hydroxyvitamin D_3 levels and poor sleep quality in a Japanese population: the DOSANCO Health Study

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Running head: Vitamin D_3 and poor sleep quality

Type of Manuscript: Original research article
Word count in Abstract/Total: 245/3247
Number of References: 47
Number of Tables/Figures: 3/0

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Abstract

Objective: The present cross-sectional study investigated the relationship between serum 25-hydroxyvitamin D_3 (25[OH]D_3) levels and the presence of poor sleep quality in a community-based Japanese adult population.

Methods: Poor sleep quality, defined as poor subjective sleep quality and/or use of sleep medication, was assessed using a self-administered questionnaire. The prevalence of poor sleep quality was compared among 512 Japanese participants aged 35 to 79 years, based on serum 25(OH)D_3 levels, which were determined using tandem mass spectrometry. A logistic regression model was used to calculate the odds ratios (ORs) for the presence of poor sleep quality in each group with the highest quartile of 25(OH)D_3 serving as the reference group.

Results: Poor sleep quality was reported by 33.2% of the total study population. The prevalence of poor sleep quality was crudely higher in the first quartile group (25[OH]D_3: 2.08–18.13 ng/mL) than in the second, third and fourth quartile groups (18.14–23.07 ng/mL, 23.08–28.32 ng/mL, and 28.33–78.83 ng/mL, respectively). The ORs for poor sleep quality were 1.86 (95% confidence interval, 1.08–3.20) for the first quartile group, 0.73 (0.41–1.29) for the second quartile group, and 0.73 (0.42–1.27) for the third quartile group after adjusting for age, sex, and sociodemographic, lifestyle, physical and environmental factors, while the ORs were 1.68 (0.96–2.95), 0.69 (0.39–1.24), and 0.65 (0.37–1.15) after further adjustment for overall health status and depression status.

Conclusions: The first quartile group of serum 25(OH)D_3 was associated with the presence of poor sleep quality.

Keywords: 25-hydroxyvitamin D_3; sleep quality; epidemiology; Japanese

1. Introduction

Sleep is an essential component of health and well-being. Complaints about sleep and associated difficulties are considerable issues in developed countries [1]. Among adults in the United States, based on the National Health Interview Survey in 2013–2015, 32.5% of males and 40.4% of females reported waking up without feeling well rested [2]. The National Health and Nutrition Survey in 2015 in Japan revealed that 19.3% and 21.6% of male and female adults, respectively, were unsatisfied with their sleep [3]. These issues concerning sleep not only increase the risk of a poor quality of life, but also can be a contributing root cause of various kinds of disorders and accidents [4-8].

Recently, interest in vitamin D as a possible substance implicated in sleep regulation has been increasing, because of the biological effects it experts on a wide variety of systems in the body [9,10]. However, the role of vitamin D in terms of sleep regulation remains largely unclear. One possible mechanism by which effects may occur is via vitamin D receptors located in the brainstem [11]. Animal experiments have shown that the presence of vitamin D receptors in several areas of the brainstem regulates aspects of sleep, including the onset and maintenance of sleep, and coordination of the sleep-wake cycle [11]. Several cross-sectional epidemiological studies have reported that low serum vitamin D levels are associated with poor quality of sleep (or relevant problems) in general populations, although sleep parameters differed among studies [12-18]. Some other clinical trials suggest supplementation with vitamin D can improve sleep [19,20].

The majority of relevant epidemiological studies have measured serum total 25-hydroxyvitamin D (25[OH]D)—or sum of 25-hydroxyvitamin D_2 and D_3 (25[OH]D_2 and 25[OH]D_3)—when assessing vitamin D in the body. However, evidence suggests the

importance of quantifying 25(OH)D_2 and 25(OH)D_3 separately when evaluating vitamin D status, although 25(OH)D_3 is the predominant form of vitamin D circulating in the blood [21,22]. Only 25(OH)D_3 is converted to 1α,25-dihydroxyvitamin D_3 in the kidneys and becomes the active form of vitamin D modulating our endocrine system [21]. The present study focused on the relationship between serum 25(OH)D_3 levels and the presence of poor sleep quality in a general population, using cross-sectional data collected from residents of a single community in Japan.

2. Methods

2.1.Study design and population

A cross-sectional study was conducted as part of the Dynamics of Lifestyle and Neighborhood Community on Health Study (DOSANCO Health Study), a community-based study conducted in the town of Suttu, Hokkaido, Japan, during 2015 [23]. Briefly, a total of 2100 participants (977 men and 1123 women) comprising 79.6% of all residents aged ≥3 years (other than those living at nursing homes), completed a self-administered questionnaire; if participants were elementary school students or younger, the questionnaire was filled out by their parents. Blood samples were requested from 729 of the 2100 participants on the basis of ages (i.e., those aged 35–79 years); 545 participants (245 men and 300 women) complied and were screened for eligibility. A total of 33 participants were deemed ineligible for inclusion because of missing data related to vitamin D (n=0), sleep status (n = 9), or characteristics other than vitamin D and sleep status (n = 24). The remaining 512 individuals (226 men and 286 women) were considered as eligible study participants and included in the subsequent analyses. The study protocol was approved by the Institutional Review Committee for Ethical

Issues of the Faculty of Medicine (15-002, 16-007) and the Faculty of Health Sciences (16-10), Hokkaido University. Written informed consent was obtained from all participants.

2.2.Data collection

Venous blood samples were collected by cubital venipuncture after an overnight fast. Serum was separated and centrifuged after blood coagulation. Serum samples were stored at −80°C until vitamin D was measured. Serum 25(OH)D_3 (ng/mL) measurements were performed at our laboratory for each study participant (Hokkaido University Faculty of Health Science) using tandem mass spectrometry (LC-MS/MS) [24].

Sleep status was assessed using the self-administered questionnaire which was extracted from the Pittsburgh Sleep Quality Index (PSQI) [25,26]. Subjective sleep quality was reported based on the responses to the following question: "*During the past month, how would you rate your sleep quality overall?*" Participants were required to select one of the four following responses that most closely represented their experience: "*very good*," "*fairly good*," "*fairly bad*," or "*very bad*." Poor subjective sleep quality was defined as "*fairly bad*" or "*very bad*" [27]. Because the parameter of sleep quality used in our study was the most influential component of the seven components making up the PSQI global score [28,29], it was considered as potentially useful for the assessment of overall sleep status without focusing on specific complaints and problems about sleep. Use of sleep medication was reported based on the responses to the following question: "*During the past month, how often have you taken medicine (prescribed or "over-the-counter") to help you sleep?*" Participants were required to select one of the four following responses that most closely represented their experience: "*not during the past month*," "*less than once a week*," "*once or twice a week*," or "*three or more times a week*." Use of sleep medication was defined as "*once or twice a week*," or "*three or*

more times a week" [27]. In this report, poor sleep quality was defined as poor subjective sleep quality and/or use of sleep medication.

Other data collected using the self-administered questionnaire included age, sex, marriage status, work status, exercise, smoking and alcohol drinking habits, overall health status, and depression status. Habitual exercise was classified as partaking in ≥10 minutes of physical exercise per day. Smoking habits were classified according to whether a participant had never smoked, was a former smoker, or was a current smoker. Habitual alcohol drinking was classified on the basis of whether a participant had never consumed an alcoholic drink, was a former drinker, or currently consuming an alcoholic drink on average <1 day per week, or was a current drinker consuming ≥1 day per week. Overall health status was reported based on the responses to the following question: "*How would you describe your physical condition?*" Participants were required to select one of the four following responses that most closely represented their experience: "*very well*," "*fairly well*," "*fairly poor*," or "*very poor*." Poor overall health was defined as "*fairly poor*" or "*very poor*." Depression status was assessed using the Patient Health Questionnaire-9 [30,31] in combination with history of depression. Participants were asked to report the frequency with which they may have experienced any of the nine types of depressive episodes during the previous two weeks; response choices were "*not at all*," "*several days*," "*more than half the days*," and "*nearly every day*." Each episode was weighted equally on a 0−3 scale for frequency, and the scores for each episode were combined to yield a summary score ranging from 0−27 points, with higher scores representing a more depressed state. Being depressed was defined as ≥10 points overall [32] and/or having a history of depression. Body height and weight were measured, and body mass index was calculated as weight (kg)/height squared (m^2). Serum creatinine level was measured by the enzymatic method. Estimated glomerular filtration rate was

calculated using the Chronic Kidney Disease Epidemiology Collaboration equation [33], modified by the Japanese coefficient [34].

2.3.Statistical analysis

Initially, we compared the prevalence of poor sleep quality in the study participants grouped according to quartiles of serum 25(OH)D_3. Although vitamin D deficiency is commonly defined as a total serum 25(OH)D concentration of <20 ng/mL [35], the clinical threshold of serum 25(OH)D_3 has not been established. Therefore, we primarily used quartiles to categorize serum 25(OH)D_3 levels. Odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were calculated for the presence of poor sleep quality using a logistic regression model for each study group categorized by quartile of serum 25(OH)D_3. The group with the highest quartile of serum 25(OH)D_3 was the reference group. The model incorporated the following covariates as potential confounding factors: age (years, as a continuous variable), sex (male or female), marriage status (yes or no), work status (yes or no), exercise habits (yes or no), smoking habits (current, former, or never smoker, using two dummy variables with never smoker as the reference), alcohol drinking habits (≥1 day per week, <1 day per week, former drinker, or never drinker, using three dummy variables with never drinker as the reference), body mass index (kg/m^2, as a continuous variable), estimated glomerular filtration rate (ml/min/1.73m^2, as a continuous variable), and months of vitamin D measurement (August–September or October–November). Vitamin D is associated with various diseases [10], some of which can disrupt sleep. Because we assumed that such diseases would be potential mediators for the association between vitamin D and poor sleep quality, the logistic regression model further incorporated the following covariates as potential mediators: overall health status (poor or well), and depression status (yes or no). In

addition, we examined the association of serum 25(OH)D_3 levels with poor subjective sleep quality and use of sleep medication separately.

Next, we compared the prevalence of poor sleep quality in the study participants grouped with reference to the common clinical threshold used for total serum 25(OH)D (serum 25(OH)D_3 concentration <20 ng/mL and ≥20 ng/mL). Similar analyses were also repeated after stratifying the study population by the absence or presence of poor overall health and/or depression, to evaluate whether the association between serum 25(OH)D_3 levels and poor sleep quality was independent of poor overall health and depression. The significance of the interaction between serum 25(OH)D_3 levels and the status of these health problems was assessed using an interaction term for the categorical variables in the multivariate-adjusted model.

Analyses were performed using Stata 15 (StataCorp LP, College Station, TX, USA). All probability values were two-tailed, and the significance level was set at $p < 0.05$.

3. Results

3.1.Characteristics of the study population

The mean age ± standard deviation of the 512 study participants was 58.5 ± 12.3 years. The median and interquartile range of serum 25(OH)D_3 concentration was 23.08 (18.14–28.33) ng/mL for the overall population. Participants classified as having poor sleep quality accounted for 33.2% of the study population. Age, sex, smoking and alcohol drinking habits, estimated glomerular filtration rate, and months of vitamin D measurement were significantly different among groups of participants categorized by serum 25(OH)D_3 ranges according to

quartile concentrations (Table 1). Poor overall health and depression tended to be higher in the first serum 25(OH)D_3 quartile group than in most of the other groups.

(Insert Table 1)

3.2.Serum 25(OH)D_3 and poor sleep quality

Among the four study groups, the prevalence of poor sleep quality was highest in the first quartile group (serum 25[OH]D_3: 2.08–18.13 ng/mL) (Table 2). The first quartile group, but not the second or third quartile groups, had a significantly higher likelihood of poor sleep quality, compared with the fourth quartile reference group after adjusting for major potential confounding factors (multivariate-adjusted OR [model 2] 1.86 [95% CI, 1.08–3.20]). The likelihood of poor sleep quality in the first quartile group was attenuated and no longer significant after further adjustment for overall health status and depression status (multivariate-adjusted OR [model 3] 1.68 [95% CI, 0.96–2.95]). When examining the association of serum 25(OH)D_3 levels with poor subjective sleep quality and use of medication separately, a similar pattern was observed for both individual sleep problems.

(Insert Table 2)

Results using the clinical threshold of 20 ng/mL showed that the serum 25(OH)D_3 <20 ng/mL group had a significantly higher likelihood of poor sleep quality compared with the serum 25(OH)D_3 ≥20 ng/mL group, after adjusting for major potential confounding factors (multivariate-adjusted OR [model 2] 1.83 [95% CI, 1.22–2.73]) (Table 3). The likelihood of poor sleep quality in the serum 25(OH)D_3 <20 ng/mL group was attenuated, but remained

significant after further adjustment for overall health status and depression status (multivariate-adjusted OR [model 3] 1.75 [95% CI, 1.15–2.66]).

(Insert Table 3)

After stratifying the study population by the absence or presence of poor overall health and/or depression, a similar pattern was observed for both subpopulations. In the subpopulation without both poor overall health and depression (n = 368), the multivariate-adjusted OR for poor sleep quality in the serum $25(OH)D_3$ <20 ng/mL group was 1.62 (95% CI, 0.97–2.69) relative to the serum $25(OH)D_3$ ≥20 ng/mL group. In the subpopulation with poor overall health and/or depression (n = 144), the corresponding OR in the serum $25(OH)D_3$ <20 ng/mL group was 1.83 (95% CI, 0.82–4.07). There was no significant interaction between serum $25(OH)D_3$ levels and the status of these health problems for poor sleep quality (p = 0.42 for the interaction).

4. Discussion

Study participants with the lowest serum $25(OH)D_3$ concentrations, 2.08–18.13 ng/mL in the first quartile group, showed a significantly higher likelihood for the presence of poor sleep quality compared with those having higher serum $25(OH)D_3$ levels in the second-to-fourth quartile groups after adjustment for major potential confounding factors, such as age, sex, and sociodemographic, lifestyle, physical and environmental factors. However, the likelihood of poor sleep quality was attenuated in the first serum $25(OH)D_3$ quartile group after further adjusting for potential mediators, such as overall health status and depression status.

To our knowledge, this is the first evidence reported on the relationship of serum 25(OH)D_3 to the presence of sleep problems in a general population. The biological effects of vitamin D occur only as a consequence of the metabolite of 25(OH)D_3 (i.e., 1α,25-dihydroxyvitamin D_3) biding to vitamin D receptors [21]. A recent study reported that serum 25(OH)D_2 was detected in 16.4% of patients at one hospital in China a low detection limit of 2.5 ng/mL [22]. Of the patients with detectable 25(OH)D_2 in serum, the proportion of 25(OH)D_2 contribution to overall 25(OH)D ranged from 1.3% to 100%, and an inverse correlation between 25(OH)D_2 and 25(OH)D_3 [22] was observed. Therefore, it was valuable to measure serum 25(OH)D_3, rather than total 25(OH)D when investigating the biological effects of vitamin D on human health. In addition, the serum concentrations of 25(OH)D_3 in our study were measured using tandem LC-MS/MS which is considered a standard methodology [21,22,24].

Several relevant studies have measured total serum 25(OH)D levels in conjunction with assessments of the overall quality of sleep based on a questionnaire same as or closely resembling the questionnaire used in this study. Ataie-Jafari et al [12] reported poor sleep quality resulting in difficulties with daily activity among approximately 1000 school students in Iran after adjustment for major potential confounding factors; the ORs (95% CIs) according to serum 25(OH)D levels of <10 ng/mL and 10–30 ng/mL were 1.472 (1.004–2.157) and 1.348 (0.917–1.982), respectively, compared with serum 25(OH)D >30 ng/mL. Jung et al [13] reported that among approximately 1500 fixed day workers in Korea sleep quality assessed by the same questionnaire used in our study was worse when serum 25(OH)D was <10 ng/mL compared with when serum 25(OH)D was ≥10 ng/mL. For poor sleep quality, defined as a PSQI global score of ≥6 points, the OR was 1.36 (1.01–1.82) when serum 25(OH)D was <10 ng/mL compared with ≥10 ng/mL after adjustment for major potential confounding factors [13]. The results of our study were crudely in accordance with the results of these previous

studies. In our study, the presence of poor sleep quality appeared to increase when serum 25(OH)D_3 was 2.08–18.13 ng/mL.

Because of the possible links between vitamin D deficiency and many diseases [10], low levels of vitamin D may result in insufficient sleep via development of diseases that present with symptoms leading to sleep disturbance. Obstructive sleep apnoea syndrome, characterized by recurrent episodes of upper airway occlusion leading to recurrent arterial hypoxaemia and sleep fragmentation/daytime sleepiness, is associated with low levels of vitamin D [36]. Restless legs syndrome, a chronic neurological movement disorder characterized by the urge to constantly move the affected body part to stop an uncomfortable sensation, is also associated with low levels of vitamin D [37]. An association between vitamin D deficiency and depression has also been reported [38]. Many other diseases that present with uncomfortable symptoms, such as pain, itching, nasal discharge, and cough can also disrupt sleep. Because of a lack of data on such diseases (except for depression), we could not identify those diseases that were more prevalent with lower levels of vitamin D. In addition, it was unclear what diseases were associated with poor sleep quality in relation to low levels of vitamin D. Alternatively, we allowed for overall health status and depression status to evaluate the dependent and independent effect of vitamin D deficiency and health problems on sleep. Despite the higher prevalence of poor overall health and depression in participants with lower serum 25(OH)D_3 levels, low levels of serum 25(OH)D_3 were likely to be associated with poor sleep quality independent of these health problems. Because we did not allow for specific sleep-related diseases linked to vitamin D deficiency, there may have been a residual effect of potential mediators on the association of interest. Additional studies are required for further elucidation.

Taken together, our study results and those of other relevant studies suggest that a strategy for the prevention and improvement of poor sleep quality is needed. Several lifestyle and environmental factors may determine vitamin D status in humans; for example, not smoking or consuming alcohol and having adequate exposure to sunlight, particularly during outdoor activities in summer season, can help to optimize the synthesis of vitamin D in the body in addition to consuming foods (i.e., fatty fish, egg yolks) and supplements rich in vitamin D [39-42]. Lifestyle and environmental factors can contribute to improvements in poor sleep quality by increasing vitamin D levels in the body. In fact, consumption of a large amount of fish has been directly related to a good quality of sleep and long duration of sleep [43,44].

The present study had several limitations. First, our study was a cross-sectional design and lacked a prospective aspect in relation to serum 25(OH)D_3 insufficiency and the development of poor sleep quality characterized by poor subjective sleep quality and/or use of sleep medication. Second, our results were derived from residents in one northern rural community of Japan. Caution should be exercised when generalizing our results. Based on lifestyle and environmental factors in this community, vitamin D was distributed to lower levels in our study population, compared with residents in other areas of Japan [42,45-47]. However, low vitamin D levels observed in this study population facilitated our investigation into the effects of a vitamin D deficiency on sleep. Third, because we only collected data on serum 25(OH)D_3 levels at a single time point, we therefore could not consider annualized serum 25(OH)D_3 levels. In addition, we only measured 25(OH)D_3, not total 25(OH)D, and therefore could not compare the two markers. Furthermore, sleep status was assessed using two simple questions at a single time point. Fourth, we did not collect data on medications leading to sleep disturbance. Finally, analyses stratified by sex were complicated by the insufficient number of

each of males and females, so that it was necessary to combine males and females to achieve valid comparisons in this study.

5. Conclusions

Serum 25(OH)D_3 levels of 2.08–18.13 ng/mL were associated with poor sleep quality in a general Japanese population, at least partially, via other health problems. For individuals experiencing poor sleep quality, it may be necessary to incorporate some lifestyle modification and alter some environmental factors known to be associated with suboptimal concentrations of vitamin D in order to improve poor sleep quality.

Acknowledgements

We express special gratitude to all participants, Suttu town municipal government officers, Suttu town clinic stuff members, and other people who were involved in the DOSANCO Health Study.

Funding

This study was supported by grants from Integration Research for Agriculture and Interdisciplinary Fields (14538261), and from the Japan Society for the Promotion of Science, KAKENHI (26670322 and 16K16272)

Conflict of Interest

None declared.

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Table 1. Characteristics of study participants from Suttu town, Hokkaido, Japan.

	Overall (N = 512)	Serum 25-hydroxyvitamin D_3 (ng/mL)				p-value for difference
		1st quartile group ≤18.13 (2.08–18.13) (n = 128)	2nd quartile group 18.14–23.07 (n = 128)	3rd quartile group 23.08–28.32 (n = 129)	4th quartile group ≥28.33 (28.33–78.83) (n = 127)	
Age (yr)	58.5 ± 12.3	55.7 ± 12.0	56.3 ± 13.0	59.9 ± 11.6	61.9 ± 11.6	<0.001
Women (%)	55.9% (286)	63.3% (81)	60.9% (78)	53.5% (69)	45.7% (58)	0.02
Married (%)	70.5% (361)	67.2% (86)	73.4% (94)	69.0% (89)	72.4% (92)	0.66
Working (%)	68.0% (348)	71.9% (92)	71.9% (92)	66.7% (86)	61.4% (78)	0.22
Regular exercise (%)	42.2% (216)	34.4% (44)	43.8% (56)	45.0% (58)	45.7% (58)	0.22
Smoking habits (%)						0.02
Never smoker	46.3% (237)	51.6% (66)	54.7% (70)	43.4% (56)	35.4% (45)	
Former smoker	32.0% (164)	25.8% (33)	25.0% (32)	34.9% (45)	42.5% (54)	
Current smoker	21.7% (111)	22.7% (29)	20.3% (26)	21.7% (28)	22.1% (28)	
Alcohol drinking habits (%)						0.03
No drinking	32.8% (168)	39.1% (50)	29.7% (38)	31.8% (41)	30.7% (39)	
Former drinker	10.4% (53)	11.7% (15)	10.2% (13)	9.3% (12)	10.2% (13)	
<1 day per week	19.9% (102)	25.8% (33)	22.7% (29)	18.6% (24)	12.6% (16)	
≥1 day per week	36.9% (189)	23.4% (30)	37.5% (48)	40.3% (52)	46.5% (59)	
Body mass index (kg/m^2)	23.9 ± 3.8	24.1 ± 4.0	23.9 ± 3.5	23.9 ± 3.8	23.6 ± 3.8	0.70
Estimated glomerular filtration rate ($ml/min/1.73m^2$)	80.8 ± 11.5	82.7 ± 10.3	82.1 ± 11.3	80.5 ± 11.4	77.8 ± 12.3	0.003
Months of vitamin D measurement (%)						<0.001
August–September	34.0% (174)	28.1% (36)	24.2% (31)	30.2% (39)	53.5% (68)	

October–November	66.0% (338)	71.9% (92)	75.8% (97)	69.8% (90)	46.5% (59)	
Poor overall health (%)	20.7% (106)	24.2% (31)	16.4% (21)	25.6% (33)	16.5% (21)	0.13
Depressed (%)	13.7% (70)	18.0% (23)	12.5% (16)	12.4% (16)	11.8% (15)	0.44

Data are the means ± standard deviations, or the % (number) of participants in that category.

One-way analysis of variance, or Chi-square test was used to compare each characteristic in each serum 25-hydroxyvitamin D_3 quartile.

Table 2. Odds ratio for poor sleep quality in participants grouped by serum 25-hydroxyvitamin D_3 quartiles.

	Serum 25-hydroxyvitamin D_3 (ng/mL)			
	1st quartile group ≤18.13 (2.08–18.13) (n = 128)	2nd quartile group 18.14–23.07 (n = 128)	3rd quartile group 23.08–28.32 (n = 129)	4th quartile group ≥28.33 (28.33–78.83) (n = 127)
Poor sleep quality				
Cases, n	61	34	34	41
Prevalence (%)	47.7	26.6	26.4	32.3
Age and sex-adjusted OR (95% CI), model 1	1.88 (1.11–3.17)	0.75 (0.43–1.30)	0.75 (0.43–1.28)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 2	1.86 (1.08–3.20)	0.73 (0.41–1.29)	0.73 (0.42–1.27)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 3	1.68 (0.96–2.95)	0.69 (0.39–1.24)	0.65 (0.37–1.15)	1.00 (Reference)
Poor subjective sleep quality				
Cases, n	50	30	31	32
Prevalence (%)	39.1	23.4	24.0	25.2
Age and sex-adjusted OR (95% CI), model 1	1.77 (1.02–3.06)	0.85 (0.47–1.52)	0.92 (0.52–1.62)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 2	1.72 (0.97–3.03)	0.83 (0.45–1.51)	0.89 (0.50–1.60)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 3	1.52 (0.84–2.76)	0.78 (0.42–1.46)	0.77 (0.42–1.42)	1.00 (Reference)
Use of sleep medication				
Cases, n	26	8	11	16
Prevalence (%)	20.3	6.3	8.5	12.6
Age and sex-adjusted OR (95% CI), model 1	2.03 (0.99–4.15)	0.50 (0.20–1.24)	0.65 (0.29–1.48)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 2	1.83 (0.87–3.88)	0.47 (0.18–1.21)	0.63 (0.27–1.46)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 3	1.58 (0.73–3.45)	0.43 (0.16–1.12)	0.57 (0.24–1.35)	1.00 (Reference)

Abbreviations: CI, confidence interval; OR, odds ratio.

Poor sleep quality was defied as poor subjective sleep quality and/or use of sleep medication.

Three different logistic regression models were used to calculate OR (95% CI) with the 4th quartile group serving as the reference group: model 1 was adjusted for age and sex; model 2 was adjusted for the same covariates used in model 1 in addition to marriage status, work status, exercise habits, smoking habits, alcohol drinking habits, body mass index, estimated glomerular filtration rate, and months of vitamin D measurement; model 3 was adjusted for the same covariates used in model 2 in addition to overall health status and depression status.

Table 3. Odds ratio for poor sleep quality in participants grouped by the threshold of 20 ng/mL for serum 25-hydroxyvitamin D_3.

	Serum 25-hydroxyvitamin D_3 (ng/mL)	
	<20 (2.08–19.99) (n = 165)	≥20 (20.00–78.83) (n = 347)
Poor sleep quality		
Cases, n	70	100
Prevalence (%)	42.4	28.8
Age and sex-adjusted OR (95% CI), model 1	1.82 (1.22–2.69)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 2	1.83 (1.22–2.73)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 3	1.75 (1.15–2.66)	1.00 (Reference)
Poor subjective sleep quality		
Cases, n	58	85
Prevalence (%)	35.2	24.5
Age and sex-adjusted OR (95% CI), model 1	1.59 (1.05–2.39)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 2	1.58 (1.04–2.40)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 3	1.49 (0.96–2.32)	1.00 (Reference)
Use of sleep medication		
Cases, n	29	32
Prevalence (%)	17.6	9.2
Age and sex-adjusted OR (95% CI), model 1	2.45 (1.39–4.30)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 2	2.35 (1.31–4.20)	1.00 (Reference)
Multivariate-adjusted OR (95% CI), model 3	2.18 (1.19–3.99)	1.00 (Reference)

Abbreviations: CI, confidence interval; OR, odds ratio.

Poor sleep quality was defied as poor subjective sleep quality and/or use of sleep medication.

Three different logistic regression models were used to calculate OR (95% CI) with the 4th quartile group serving as the reference group: model 1 was adjusted for age and sex; model 2 was adjusted for the same covariates used in model 1 in addition to marriage status, work status, exercise habits, smoking habits, alcohol drinking habits, body mass index, estimated glomerular filtration rate, and months of vitamin D measurement; model 3 was adjusted for the same covariates used in model 2 in addition to overall health status and depression status.