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ORIGINAL ARTICLE

Sleep problems and subjective cognitive complaints among middle-aged and older adults in 45 low- and middle-income countries

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Abstract

Background Currently, a small body of evidence suggests that sleep problems are positively associated with subjective cognitive complaints (SCC). However, no studies on this topic exist from low- and middle-income countries (LMICs). Thus, we investigated the association between sleep problems and SCC in a large sample of middle-age and older adults from 45 LMICs.

Methods Cross-sectional, predominantly nationally representative, community-based data were analyzed from the World Health Survey. Sleep problems (such as difficulties falling asleep, waking up frequently during the night or waking up too early in the morning) in the last 30 days were self-reported. Two questions on subjective memory and learning complaints in the past 30 days were used to create a SCC scale ranging from 0 (No SCC) to 100 (worse SCC). Multivariable linear regression was conducted to explore the association between sleep problems (exposure) and SCC (outcome).

Results Data on 60,228 adults aged ≥ 50 years were analyzed [mean (SD) age 61.4 (9.9) years; 53.9% females]. After adjustment for potential confounders, compared to those without sleep problems, the mean SCC score for the multivariable model was 13.32 (95% CI 12.01, 14.63), 19.46 (95% CI 17.95, 20.98), 24.17 (95% CI 22.02, 26.33), and 31.39 (95% CI 28.13, 34.65) points higher for mild, moderate, severe, and extreme sleep problems, respectively. Similar results were found for analyses stratified by age and country-income level.

Conclusion Sleep problems were positively associated in a dose–response manner with SCC among middle-aged and older adults in multiple LMICs. Addressing sleep problems may aid in the prevention of SCC and ultimately dementia, pending future longitudinal research.

Keywords Sleep problems · Subjective cognitive complaints · Low- and middle-income countries · Older adults

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Introduction

Dementia is a syndrome in which there is deterioration in memory, thinking, behavior, and the ability to perform everyday activities [1]. Dementia is most common among older adults with 5–8% of the global population aged ≥ 60 years reported to have dementia [1], and almost 60% of those with dementia live in low- and middle-income countries (LMICs) [1]. Subjective cognitive complaints (SCC) refer to everyday concerns (e.g., in relation to memory and/or other cognitive functions) cited by people both with and without objective evidence of cognitive impairment [2], and has been found to be a strong predictor of dementia.

One systematic review consisting of 17 studies found that SCC (compared to no SCC) were associated with a significantly higher risk of progression to dementia [3], while, another meta-analysis suggested that older people with subjective memory complaints with no objective deficits are twice as likely to develop dementia as individuals without subjective memory complaints [4]. Furthermore, based on another review, it was concluded that individuals with SCC are at increased risk of progression to Alzheimer's disease, and that there is evidence that those with SCC have a higher prevalence of positive biomarkers for amyloidosis and neurodegeneration [5].

Interestingly, sleep problems may lead to poor cognition via, for example, abnormalities in sleep architecture that interferes with sleep-dependent memory consolidation, thus contributing to memory impairment [6]. In one study of 351 African American older adults, it was found that worse overall sleep quality was significantly associated with subjective reports of difficulty recalling the placement of objects, recalling specific facts from reading materials, and worse memory currently compared to the past. Specifically, participants classified as poor sleepers (Pittsburgh Sleep Quality Index [PSQI] total score > 5) were more likely to report worse current memory compared to the past than participants classified as good sleepers (PSQI total score ≤ 5) [7]. In another study consisting of 1011 subjects aged 65 years from France, a significant association was found between subjective cognitive and sleep complaints, and daytime sleepiness [8]. Furthermore, a study including 2962 US middle to older age adults found that people with SCC were more likely to have sleep apnea or other sleep disturbances [9].

To the authors' knowledge, no other studies exist on the association between sleep problems and SCC. It is worth noting that the existing literature has key shortcomings. First, all studies were carried out in high-income settings, despite the fact that the majority of people with dementia live in LMICs [1]. It has been suggested that use of domestic and public lighting and other environmental factors related to the sleep site shape sleep patterns [10]. Thus, it is possible that findings from high-income countries are not generalizable to LMICs, which are environmentally distinct with generally much higher proportions of rural populations [11]. Next, all studies have utilized relatively small sample sizes [7–9] and are single country studies [7–9]. Multi-country studies consisting of large and representative samples are required as multi-country studies allow for the comparison of standardized estimates across different settings.

Given this background, the aim of the present study was to investigate the association between sleep problems and SCC in a sample of 60,228 adults aged ≥ 50 years from 45 LMICs.

Methods

The World Health Survey (WHS) was a cross-sectional survey carried out in 70 countries in 2002–2004. Single-stage random sampling was undertaken in 10 countries, while stratified multi-stage random cluster sampling was conducted in 60 countries. Survey details are available elsewhere (http://www.who.int/healthinfo/survey/en/). In brief, individuals with a valid home address aged ≥ 18 years were eligible to participate. Kish tables were used so that all household members had an equal chance of being selected. The questionnaire was subject to standard translation procedures to ensure comparability. Information was obtained through face-to-face interviews and telephone interviews conducted by trained interviewers. Across all countries, the individual response rate was 98.5% [12]. To adjust for non-response, sampling weights were generated using the population distribution as reported by the United Nations Statistical Division. Ethical approval for the survey was provided by ethical boards at each study site. All participants gave their informed consent.

Subjective cognitive complaints (SCC)

SCC were assessed with two questions: (a) Overall in the last 30 days, how much difficulty did you have with concentrating or remembering things?; and (b) In the last 30 days, how much difficulty did you have in learning a new task (for example, learning how to get to a new place, learning a new game, learning a new recipe etc.)? [13]. Each item was scored on a five-point scale: none (code = 1), mild (code = 2), moderate (code = 3), severe (code = 4), and extreme/cannot do (code = 5). Since these answer options were an ordered categorical scale, as in previous WHS studies, we conducted factor analysis with polychoric correlations to incorporate the covariance structure of the answers provided for

individual questions measuring a similar construct [14–17]. The principal component method was used for factor extraction, while factor scores were obtained using the regression scoring method. The choice of a one factor solution was justified by the high eigenvalue of the first factor and the high communalities of the original variables. These factor scores were later converted to scores ranging from 0–100 to create a SCC scale with higher values representing more severe cognitive complaints.

Sleep problems

Sleep problems were assessed by the question: "Overall in the last 30 days, how much of a problem did you have with sleeping, such as falling asleep, waking up frequently during the night or waking up too early in the morning?", with answer options "None", "Mild", "Moderate", "Severe", and "Extreme". For some specific analyses, we used a dichotomized variable of severe/extreme or not [18].

Control variables

The control variables were selected based on past literature [7], and included age, sex, highest level of education achieved (no formal, primary, secondary, tertiary), depression, and perceived stress. Depression referred to having had past 12-month depression assessed by questions from the World Mental Health Survey version of the Composite International Diagnostic Interview [19]. Stress over the month prior to the interview was assessed by two questions from the Perceived Stress Scale [20]: "How often have you felt that you were unable to control the important things in your life?"; and "How often have you found that you could not cope with all the things that you had to do?" The answer options to these questions were: never (score = 1), almost never (score = 2), sometimes (score = 3), fairly often (score = 4), very often (score = 5). Factor analysis with polychoric correlations was conducted to create a scale ranging from 0 to 100 with higher scores representing greater levels of stress.

Statistical analysis

Data were publicly available for 69 countries. Of these, 10 countries were excluded due to a lack of sampling information. Furthermore, 10 high-income countries were excluded to focus on LMICs. Moreover, Turkey was deleted due to lack of data on education, while Brazil, Hungary, and Zimbabwe were omitted due to lack of data on perceived stress. Thus, the final sample consisted of 45 LMICs according to the World Bank classification at the time of the survey (2003). The data were nationally representative for all countries with the exception of China, Comoros, the Republic of Congo, Ivory Coast, India, and Russia.

Statistical analyses were performed with Stata 14.1 (Stata Corp LP, College station, Texas). The analysis was restricted to those aged ≥ 50 years to focus on the middle-aged (i.e., 50–64 years) and older (≥ 65 years) population. The middle-aged was also included in our study as from the point of prevention of dementia, intervening in middle-age is now considered important [21], especially that cognitive dysfunction can manifest up to 10 years before a dementia diagnosis [22].

Multivariable linear regression analysis was conducted to assess the association between sleep problems (exposure) and SCC score (outcome). Analyses were conducted for the overall sample and also for age (50–64 and ≥ 65 years) or country-income level (low-income countries and middle-income countries) stratified samples. This analysis used the five-category sleep problems variable (i.e., none, mild, moderate, severe, extreme). Next, country-wise multivariable linear regression analysis was conducted to assess the association between severe/extreme sleep problems (exposure) and SCC score (outcome). Analyses using the overall sample and samples by age group were conducted. To assess the between-country heterogeneity that may exist in these associations, we calculated the Higgins' I^2 based on estimates for each country. The Higgins' I^2 represents the degree of heterogeneity that is not explained by sampling error with a value of < 40% often considered as negligible and 40–60% as moderate heterogeneity [23]. The pooled estimate overall and by country-income levels was obtained by meta-analysis with random effects.

All regression analyses were adjusted for age, sex, education, depression, perceived stress, and country with the exception of the country-wise analysis which was not adjusted for country. Adjustment for country was done by including dummy variables in the models as in previous WHS publications [24, 25]. The sample weighting and the complex study design were taken into account in all analyses. Results from the linear regressions are presented as b-coefficients with 95% confidence intervals (CIs). The level of statistical significance was set at $P < 0.05$.

Results

The analytical sample included 60,228 adults aged ≥ 50 years from 45 LMICs (age 50–64 years $n = 30{,}868$; age ≥ 65 years $n = 23{,}360$). The included countries and their sample sizes are provided in Table S1 of the Appendix. The sample characteristics are provided in Table 1. The mean (SD) age was 61.4 (9.9) years and 53.9% were females. The prevalence of sleep problems overall was 24.3% (mild), 18.4% (moderate), 11.8% (severe), and 2.4% (extreme). The mean SCC score increased linearly with increasing severity of sleep problems

Table 1 Sample characteristics (overall and by age)

Characteristic	Overall	Age	
		50–64 years	≥ 65 years
Age (years)			
Mean (SD)	61.4 (9.9)	55.6 (4.4)	72.1 (7.0)
Sex			
Female	53.9	52.6	56.2
Male	46.1	47.4	43.8
Education			
No formal	40.3	39.7	41.5
Primary	27.2	26.3	28.7
Secondary	24.2	24.7	23.4
Tertiary	8.3	9.3	6.4
Depression			
No	90.4	91.7	88.1
Yes	9.6	8.3	11.9
Perceived stress[a]			
Mean (SD)	40.6 (29.3)	39.2 (28.2)	43.3 (31.1)
SCC score[b]			
Mean (SD)	33.1 (31.7)	27.5 (28.9)	43.3 (34.0)
Sleep problems			
None	43.1	48.4	33.3
Mild	24.3	24.2	24.4
Moderate	18.4	16.1	22.6
Severe	11.8	9.3	16.4
Extreme	2.4	1.9	3.3

SCC subjective cognitive complaints, *SD* standard deviation

Data are % unless otherwise stated

[a]The perceived stress score ranged from 0 to 100 with higher scores representing greater perceived stress

[b]The outcome (subjective cognitive complaints score) ranged from 0 to 100 with higher scores representing greater cognitive complaints

regardless of age group (Fig. 1). The mean SCC score was 19 in those without sleep problems, but this increased to 65.4 in those with extreme sleep problems. After adjustment for several potential confounders, compared to those without sleep problems, the mean SCC score was 13.32 (95% CI 12.01, 14.63), 19.46 (95% CI 17.95, 20.98), 24.17 (95% CI 22.02, 26.33), and 31.39 (95% CI 28.13, 34.65) points higher for mild, moderate, severe, and extreme sleep problems, respectively (Table 2). Similar results were found for analyses stratified by age and country-income level. The country-wise association between severe/extreme sleep problems and SCC score in adults aged ≥ 50 years is shown in Fig. 2. The pooled estimate for all countries was 13.96 (95% CI 12.47–15.45) with a moderate level of between-country heterogeneity ($I^2 = 58.6\%$). Pooled estimates for low-income countries and middle-income countries were 15.93 (95% CI 13.42, 18.43; $I^2 = 63.6\%$) and 12.55 (95% CI 10.82, 14.27; $I^2 = 47.9\%$), respectively. The estimates for those aged 50–64 years (Fig. S1 of the Appendix) and ≥ 65 years (Fig. S2 of the Appendix) were similar.

Discussion

Main findings

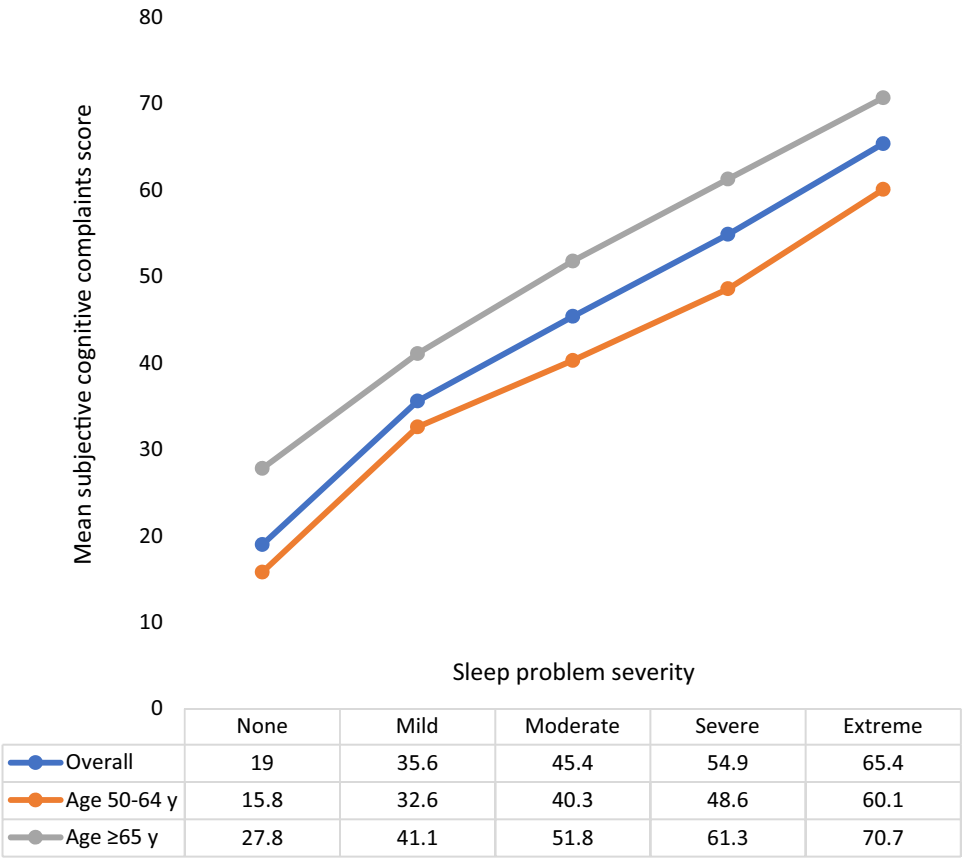
In this large predominantly nationally representative sample of adults aged ≥ 50 years from 45 LMICs, in the multivariable linear regression model, it was found that compared to those without sleep problems, the mean SCC score was 13.32 (95% CI 12.01–14.63), 19.46 (95% CI 17.95–20.98), 24.17 (95% CI 22.02–26.33), and 31.39 (95% CI 28.13–34.65) points higher for mild, moderate, severe, and extreme sleep problems, respectively. The results were similar for middle-aged and older adults. Furthermore, severe/extreme sleep problems were significantly associated with worse SCC in most individual countries included in the study.

Interpretation of findings

Findings from the present study both support the limited previous literature by confirming that an association exists between sleep problems and SCC [7–9], and add to the existing literature by demonstrating for the first time that such an association also holds among middle-aged and older adults in a very large sample across multiple LMICs.

There are several plausible pathways that likely explain the relationship between sleep problems and SCC. First, sleep problems (specifically short sleep duration) have been found to be associated with greater age-related brain atrophy and cognitive decline 2 years later [26]. Such brain atrophy may be owing to sleep problems resulting in shrinkage of large neurons, loss of myelinated axonal fibers, deafferentation, and reduction in synaptic density [27, 28]. Second, sleep has been found to facilitate overnight memory consolidation, and sleep problems can thus inhibit this process [29]. Third, sleep problems are associated with a poor diet (e.g., higher intakes of confectionary and sugar) and lower levels of physical activity [30, 31], both of which have been implicated in SCC [32, 33]. Indeed, sleep problems may lead to poor diet owing to stimulating hunger and/or suppressing satiety signals. Insufficient sleep leads to orexigenic changes in both subjective and objective measures of hunger and fullness [30]. Moreover, poor sleep may lead to lower levels of physical activity owing to fatigue; however, this hypothesis has yet to be investigated.

Interestingly, although a positive association between severe/extreme problems and SCC was observed across all countries included in the study, the strength of the association was moderately different ($I^2 = 58.6\%$). Overall, the strength of the association was stronger in low-income



	None	Mild	Moderate	Severe	Extreme
Overall	19	35.6	45.4	54.9	65.4
Age 50-64 y	15.8	32.6	40.3	48.6	60.1
Age ≥65 y	27.8	41.1	51.8	61.3	70.7

Fig. 1 Mean subjective cognitive complaints score by severity of sleep problems. The subjective cognitive complaints score ranged from 0 to 100 with higher scores representing greater cognitive complaints

countries than in middle-income countries, but country-income level may not be a main determinant of the between-country heterogeneity as there was a moderate level of heterogeneity within low-income or middle-income countries. Previous studies have shown that technological, demographic, cultural and geographical differences may influence sleep quality and its association with health status at the population level [11]. Thus, it is possible that sleep problems are associated with other behavioral factors which can lead to greater SCC (e.g., lower physical activity, poor diet) differentially by setting or that this may be explained by the proportion of people who are taking medications to facilitate sleep (e.g., benzodiazepines), which have been reported to be associated with cognitive impairment [34]. However, future studies are warranted to understand the reason why the magnitude of the association differs by country.

Public health and clinical implications

Data from the present study suggest that sleep problems in LMICs are associated with SCC, and that addressing sleep problems may reduce risk for SCC, although future longitudinal studies are warranted. In a recent meta-analysis, it was concluded that interventions targeting cognitive and behavioral self-regulation (e.g., stress management/relaxation; meditation; controlled breathing; and stimulus control) improves sleep quality in adults without clinical sleep disorder [35]. Future studies should assess which type of intervention would be most suitable for LMICs where resources are limited. This is likely to improve other parameters of population health as sleep problems or insomnia have been associated with other adverse health outcomes such as increased risk for cardiovascular disease [36].

Moreover, clinicians should be aware of the high risk for SCC among those with sleep problems and attempt to address sleep problems whenever possible in middle-aged and older adults to prevent SCC, as SCC are not only associated with higher risk for dementia but other deleterious outcomes such as lower quality of life [37], fractures, falls, increased health care utilization [38], and premature mortality [39]. Finally, SCC can identify subtle changes in everyday functioning that could be a precursor for more serious cognitive decline and functioning, which may not be detected otherwise, and can more easily be measured than objective cognitive function [40]. Thus, this can be a potentially useful tool to identify people with sleep problems who are at increased risk for cognitive decline especially in LMICs where resources are limited, pending future research. Finally, although the present study focused exclusively on LMICs, the overarching body of literature indeed suggests

Table 2 Association between sleep problems (or covariates) and subjective cognitive complaints (outcome) estimated by multivariable linear regression

Characteristic	Overall	Age 50–64 years	Age ≥ 65 years	LICs	MICs
Sleep problems					
None	Ref.	Ref.	Ref.	Ref.	Ref.
Mild	13.32**	14.50**	10.90**	14.59**	11.33**
	[12.01, 14.63]	[12.96, 16.05]	[7.87, 13.92]	[12.61, 16.57]	[10.00, 12.66]
Moderate	19.46**	19.61**	18.63**	19.13**	19.50**
	[17.95, 20.98]	[17.93, 21.30]	[15.44, 21.82]	[16.78, 21.48]	[17.89, 21.12]
Severe	24.17**	24.38**	23.08**	26.25**	21.49**
	[22.02, 26.33]	[21.78, 26.98]	[19.07, 27.10]	[23.34, 29.16]	[18.45, 24.52]
Extreme	31.39**	31.96**	29.93**	30.65**	32.63**
	[28.13, 34.65]	[27.39, 36.53]	[24.82, 35.05]	[25.94, 35.36]	[28.96, 36.29]
Age (years)	0.59**	0.50**	0.58**	0.60**	0.59**
	[0.53, 0.64]	[0.37, 0.63]	[0.43, 0.73]	[0.51, 0.68]	[0.53, 0.65]
Sex					
Female	Ref.	Ref.	Ref.	Ref.	Ref.
Male	− 4.80**	− 4.92**	− 4.59**	− 6.22**	− 2.91**
	[− 6.09, − 3.51]	[− 6.09, − 3.76]	[− 7.00, − 2.19]	[− 8.32, − 4.12]	[− 3.94, − 1.88]
Education					
No formal	Ref.	Ref.	Ref.	Ref.	Ref.
Primary	− 4.07**	− 3.32**	− 5.59**	− 4.15**	− 2.43*
	[− 5.44, − 2.70]	[− 5.00, − 1.64]	[− 8.42, − 2.75]	[− 5.78, − 2.51]	[− 4.53, − 0.33]
Secondary	− 7.01**	− 6.67**	− 7.87**	− 5.69**	− 6.09**
	[− 8.60, − 5.42]	[− 8.61, − 4.72]	[− 11.42, − 4.31]	[− 7.89, − 3.49]	[− 8.50, − 3.67]
Tertiary	− 11.38**	− 10.49**	− 12.09**	− 12.16**	− 9.54**
	[− 13.64, − 9.13]	[− 12.87, − 8.10]	[− 16.45, − 7.73]	[− 15.29, − 9.02]	[− 12.67, − 6.40]
Depression					
No	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	8.77**	9.77**	6.96**	9.47**	7.32**
	[6.72, 10.81]	[7.52, 12.03]	[3.75, 10.18]	[6.59, 12.34]	[5.14, 9.51]
Perceived stress[a]	0.16**	0.15**	0.19**	0.14**	0.19**
	[0.14, 0.19]	[0.12, 0.17]	[0.15, 0.23]	[0.11, 0.18]	[0.17, 0.22]

LICs low-income countries; MICs middle-income countries; Ref reference category

Data are b-coefficients [95% confidence intervals]

Models are adjusted for all variables in the respective columns and country

The outcome (subjective cognitive complaints score) ranged from 0 to 100 with higher scores representing greater cognitive complaints

[a] The perceived stress score ranged from 0 to 100 with higher scores representing greater perceived stress

* $P < 0.05$, ** $P < 0.001$

that it is important to examine the relationship between sleep problems and SCCs, and address these problems independently of country-income level.

Strength and limitations

The large predominantly nationally representative sample of middle-aged and older adults from 45 LMICs are clear strengths of the present study. However, findings must be interpreted considering the study limitations. First, the study was cross-sectional in nature, and the direction of the association cannot be confirmed. For example, it may be possible that SCC leads to worries, and in turn, this may disturb sleep. Future studies of a longitudinal nature are required to investigate the direction of the association. Second, sleep problems and SCC were both self-reported, potentially introducing reporting bias into the findings. Third, data on different types of sleep problems were not collected and it may be that the sleep problem-SCC relationship may differ depending on the type of sleep problem. Finally, two questions on SCC were used in our study but there is currently no consensus on the best measure for SCC, and previous

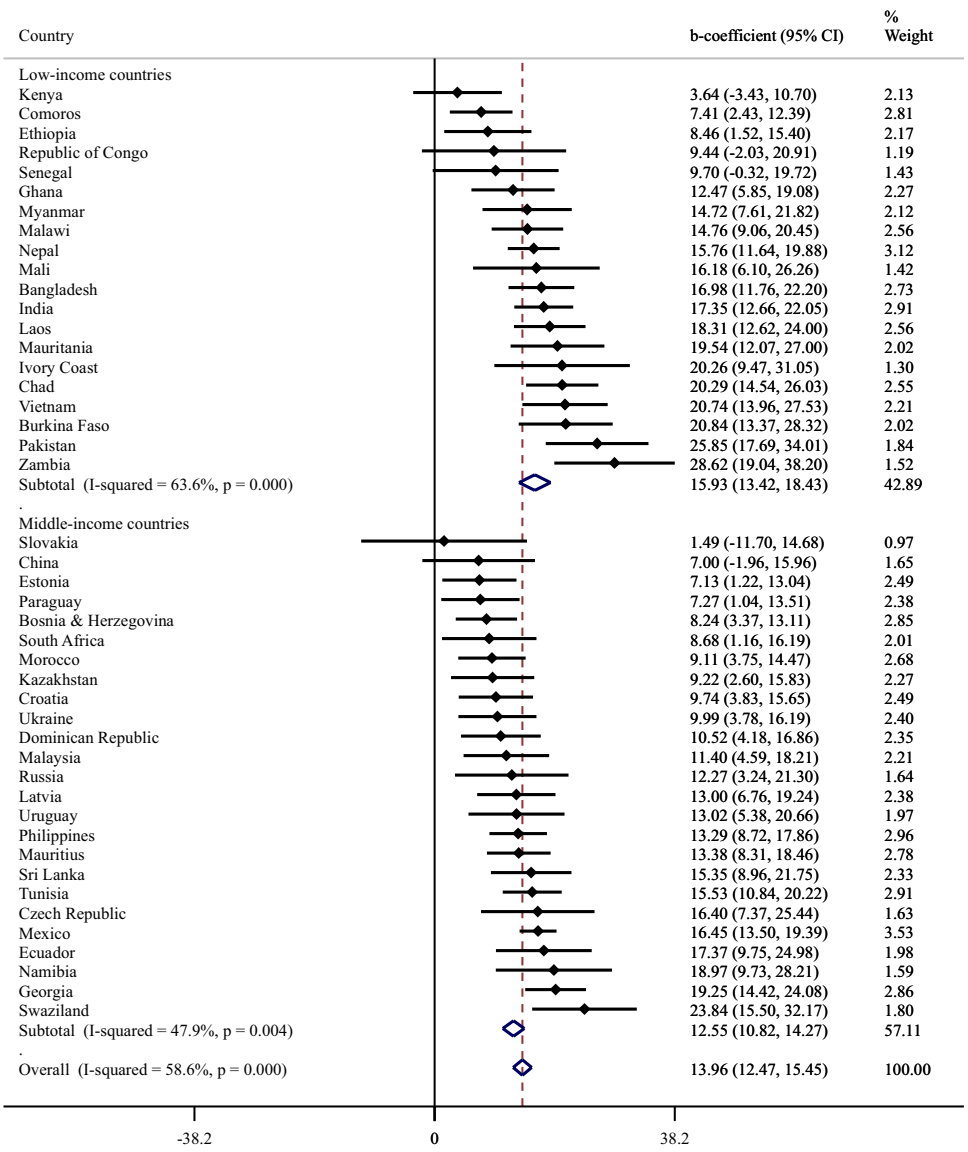


Fig. 2 Country-wise association between severe/extreme sleep problems (exposure) and subjective cognitive complaints score among adults aged ≥ 50 years estimated by multivariable linear regression. *CI* Confidence interval. The subjective cognitive complaints score ranged from 0 to 100 with higher scores representing greater cognitive complaints. Models are adjusted for age, sex, education, depression, and perceived stress. Overall estimate was obtained by meta-analysis with random effects

studies have used a single question to a complex assessment involving multiple questions. Therefore, the use of a different measure of SCC could have yielded different results.

Conclusion

In this large sample of adults aged ≥ 50 years from 45 LMICs, it was found that sleep problems were positively associated with SCC. If confirmed by longitudinal studies, addressing sleep problems may aid in the prevention of SCC and ultimately dementia.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40520-021-02052-1.

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Declarations

Conflict of interest None.

Ethical standards The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Ethical approval Ethical approval for the survey was provided by ethical boards at each study site.

Statement of human and animal rights All human and animal studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent All participants gave their informed consent.

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