Physical inactivity amplifies the negative association between sleep quality and depressive symptoms

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Abstract

Poor sleep quality and physical inactivity are risk factors for depressive symptoms. Yet, whether these factors differently contribute to depressive symptoms and whether they interact with one another remains unclear. This study aimed to examine how sleep quality and physical activity influence depressive symptoms. 79,274 adults who were 50 years of age or older (52.4% women) and responded to the Survey of Health, Ageing and Retirement in Europe (SHARE) were included in the study. Sleep quality (poor vs. good), physical activity (inactive vs. active), and depressive symptoms (0-to-12 score) were repeatedly (7 waves of data collection) collected between 2004 and 2017. The effects of sleep quality and physical activity on depressive symptoms and their interaction were tested using linear mixed-effects models. Results showed that **s**leep quality and physical activity both showed associations with depressive symptoms. Specifically, participants with poorer sleep quality reported more depressive symptoms than participants with better sleep quality (b = 1.85, 95% CI = 1.83 – 1.86, $p < .001$). Likewise, physically inactive participants reported more depressive symptoms than physically active participants (b = 0.44, 95% CI = 0.42 – 0.45, $p < .001$). Moreover, sleep quality and physical activity showed an interactive association with depressive symptoms (b = 0.17, 95% CI = 0.13 – 0.20, $p < .001$). The negative association between sleep quality and depressive symptoms was stronger in physically inactive than physically active participants. These findings suggested that, in adults 50 years of age or older, both sleep quality and physical activity are related to depressive symptoms. Moreover, the detrimental association between poor sleep quality and depressive symptoms is amplified in physically inactive individuals.

Keywords: sleep quality, physical activity, depression, aging

Introduction

Depression is a mental disorder affecting over 300 million people[1] and a leading cause of disability worldwide.[2] Depressive symptoms include persistent feeling of sadness, fatigue or loss of interest, diminished appetite, sleepiness, and worthlessness.[3 4] These symptoms have a major impact on quality of life and daily functioning,[5] and their prevalence increases with age.[6] Depression affects 7% of the world's older population[7 8] and increases the risk for detrimental health-related outcomes in this population, including all-cause cardiovascular and stroke mortality,[2 9 10] coronary diseases,[11 12] insulin resistance,[13] and overweight.[2 14] Moreover, depression is associated with cognitive and functional impairment, as well as social dysfunction.[15] Improving our understanding of the factors influencing depressive symptoms can contribute to their prevention and treatment. Recently, modifiable lifestyle behaviors such as sleep quality and physical activity have proved to be important factors in the development of depressive symptoms.[16 17]

Both poor sleep quality and physical inactivity have been associated with negative health outcomes including depressive symptoms.[16-24] For example, studies have shown a non-linear association between sleep duration and depressive symptoms, with the highest risk of depressive symptoms being observed when sleep duration was below 4 or 6 hours per night.[25 26] Likewise, a recent study showed that older adults accumulating at least 3,500 steps per day demonstrated a reduced risk of developing depressive symptoms, with 7,000 steps per day providing the highest protective effect.[16] Besides the demonstrated effects of physical activity and sleep quality on depressive symptoms, previous research has suggested a potential interaction between these two effects, but current evidence is scant.[27 28] The closest experimental result we could find concerning such an interaction was from Bellavia et *al.*, who showed that long sleep duration (i.e., > 8 hours per night), which may represent an epiphenomenon of comorbidity,[29] was associated with an increased risk of mortality, but only among individuals reporting low usual levels of physical activity.[30] Similarly, a recent study showed that the deleterious associations of poor sleep quality with all-cause and cause-specific mortality were amplified by physical inactivity,[31] although the association with all-cause mortality was not observed in another large-scale study.[27] To the best of our knowledge, however, no study has yet directly examined the potential interactive effect of sleep quality and physical activity with depressive symptoms

To address this knowledge gap, we analyzed data obtained by a large-scale longitudinal study aimed to investigate the effects of sleep quality, physical activity, and their interaction on depressive symptoms in European adults 50 years of age or older. Based on the literature supporting an interaction of these two effects on mortality,[30 31] we hypothesized that the negative association between sleep quality and depressive symptoms is exacerbated by physical inactivity.

Methods

Study design

The Survey of Health, Ageing and Retirement in Europe (SHARE) is a prospective cohort study of 140,000 adults aged 50 years or older living in 27 European countries and Israel. Participants completed questionnaires, in-depth interviews, and tests (e.g., cognitive and physical measurements) every two years between 2004 and 2017 (7 waves of data collection). Physical activity, sleep, and depressive symptoms were assessed in all waves of measurements, with the exception of wave 3. SHARE was carried out in accordance with the Declaration of Helsinki and has been approved by the Ethics Committee of the University of Mannheim (waves 1-4) and the Ethics Council of the Max Plank Society (waves 4-7). All participants provided a written informed consent. Detailed methods are described elsewhere.[32]

To be included in the study, participants should be 50 to 96 years of age and have at least one measure of physical activity, sleep quality, and depressive symptoms. To reduce reverse causation bias,[33] we excluded participants with a suspicion of depression at baseline as indicated by scores ≥ 4 on the EURO-D scale.[34 35]

Measures

Outcome: Depressive symptoms. Depressive symptoms were measured using the EURO-D scale, which includes 12 items capturing the presence or absence of depressed mood, pessimism, wishing death, guilt, sleep, interest, irritability, appetite, fatigue, concentration, enjoyment, and tearfulness. Each item was coded 1 (symptom present) or 0 (symptom absent) to generate a score ranging from 0 to 12, with higher scores reflecting more depressive symptoms. The EURO-D scale has been found to be reliable and valid to measure late-life depression.[34 35] Note that we conducted a robustness in which the depressive symptoms score was calculated without the item measuring sleep trouble (see robustness analysis section).

Predictors: Sleep quality and physical activity.

Sleep quality was derived from the question "Have you had trouble sleeping recently?" Participants who answered "Trouble with sleep or recent change in pattern" were classified as having a poor sleep quality, whereas participants who answered "No trouble sleeping" were classified as having a good sleep quality.[36]

Physical Activity was derived from the following two questions: "We would like to know about the type and amount of physical activity you do in your daily life. How often do you engage in vigorous physical activity, such as sports, heavy housework, or a job that involves physical labor?" and "How often do you engage in activities that require a low or moderate level of energy such as gardening, cleaning the car, or doing a walk?".[37-39] Participants answered using a four-point scale: 1 = *Hardly ever, or never*; 2 = *One to three times a month*; 3 = *Once a week*; 4 = *More than once a week*. Participants who did not answer "more than once a week" to either item were classified as physically inactive, whereas the other participants were categorized as physically active. As described in previous research,[40] this strategy reduces the potential misclassification bias that would lead physically inactive participants being incorrectly classified as physically active.

Covariates and potential confounders. To reduce the influence of potential confounding factors on the associations of sleep and physical activity with depressive symptoms, demographic, socio-economic, and health covariates were selected based on the literature. These covariates included *wave of measurement* (from wave 1 to 7), *age* (50-64; 65-79; 80-96), *sex* (male, female), *body mass index* (underweight: <18.5, normal: ≥18.5 and <25, overweight: ≥25 and <30, obese: ≥30 kg/m^2), *education* (seven categories based on the International Standard Classification of Education),[41] *ability to make ends meet* (with great difficulty, with some difficulty, fairly easily, easily), *cognitive functions* (delayed recall and verbal fluency), *birth cohort* (between 1919 and 1928, between 1929 and 1938, between 1939 and 1945, after 1945), *country of residence* (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Luxembourg, Netherlands, Poland, Portugal, Slovenia, Spain, Sweden, Switzerland), *attrition* [no dropout, dropout (participants who responded to neither wave 6 nor wave 7), death] and *number of chronic diseases* (fewer than two chronic conditions, two or more chronic conditions).

Statistical analyses
All analyses were performed using R version 4.0.3 and were two-sided.[42] Descriptive statistics are presented stratified by sleep quality. Linear mixed-effects models were conducted to examine the association between sleep and physical activity with depressive symptoms as well as their interaction using the lme4 and lmerTest packages.[43 44] Mixed-effects models account for the nested structure of the data (i.e., repeated measurement over time within a single participant) and provide acceptable type I error rates.[45] Moreover, participants with missing observations can be included as these models do not require an equal number of observations across participants.[46]

Two sets of mixed-effects models were performed, with physically active and good sleep quality serving as the reference categories. Model 1 tested the associations of sleep and physical activity with depressive symptoms. Model 2 tested the interaction between the two primary exposures (i.e., sleep and physical activity). Each of these mixed-effects models were first minimally adjusted by including wave of measurement, age, and sex as covariates. Models were then further adjusted for body mass index, education, ability to make ends meet, cognitive functions, birth cohort, country of residence, attrition, and number of chronic diseases. Finally, to allow each participant to have their own evolution of depressive symptoms across waves, the models included a random effect of wave at the level of the participant.

Sensitivity and robustness analyses
Two sensitivity analyses were conducted. In the first sensitivity analysis, participants who dropped out during the survey were excluded. In the second sensitivity analysis, participants who died during the survey were excluded. These analyses were conducted to minimize selective attrition bias as participants who dropped out or died during the follow-up were likely to have specific characteristics that may bias the associations observed.

Three robustness analyses were conducted. In the first robustness analysis, we introduced a time lag between the exposures (i.e., physical activity and sleep quality) and the outcome (i.e., depressive symptoms) to minimize the impact of reverse causation bias on the associations observed. Specifically, the predictors were assigned the value of the preceding wave,[47] which is equivalent to a time lag of approximately two years. In the second robustness analysis, the item measuring sleep trouble in the EURO-D scale was excluded to avoid a potentially inflated association between sleep quality and depressive symptoms. The third robustness analysis was also based on the 11-item EURO-D scale. In addition, the threshold for being considered physical active was lowered. Participants who answered "one to three times a month" to either the moderate or the vigorous items were classified as physically active, whereas only participants who answered "hardly ever, or never" to both items were classified as physically inactive.

Results

Descriptive statistics by sleep quality at baseline
A total of 79,274 participants (57, 36, and 7% were 50-64, 65-79, and 80-96 years of age, respectively; 52% women) were included in the study sample. The majority of the participants reported being physically active (73%) and having a good sleep quality (70%). Table 1 presents the characteristics of the participants stratified by sleep quality at baseline. Simple association tests showed better sleep quality in participants who were less depressed, physically active, younger, women, with a lower body mass index, had advantaged socioeconomic status, faced fewer chronic conditions, and had better cognitive functions (*ps* <.001).

Table 1. Baseline characteristics of the participants stratified by sleep quality

	Poor sleep quality (N = 24,003)	Good sleep quality (N = 55,271)	*P* value
Outcome			
Depressive symptoms, mean ± SD	3.4 ± 1.8	1.4 ± 1.5	<0.001
Exposure			
Physical activity, n (%)			
Physically active	16947 (71)	41467 (75)	
Physically inactive	7051 (29)	13804 (25)	<0.001
Other covariates			
Age, n (%)			
50-64	12983 (54.1)	32266 (58)	
65-79	9138 (38.1)	19254 (35)	
80-96	1882 (7.8)	3751 (7)	<0.001
Sex, n (%)			
Women	15239 (63)	26362 (48)	
Men	8764 (37)	28909 (52)	<0.001
Body mass index, n (%)			
Underweight	324 (1)	558 (1)	
Normal weight	8588 (36)	20411 (37)	
Overweight	9629 (40)	23601 (43)	
Obesity	5462 (23)	10701 (19)	<0.001
Education, n (%)			
Primary	5572 (23)	12285 (22)	
Secondary	13541 (57)	30262 (55)	
Tertiary	4890 (20)	12724 (23)	<0.001
Ability to make ends meet			
With great difficulty, n (%)	2466 (10)	4495 (8)	
With some difficulty, n (%)	5376 (23)	10896 (20)	
Fairly easily, n (%)	7447 (31)	17348 (31)	
Easily, n (%)	8714 (36)	22532 (41)	<0.001
Cognitive functions			
Delayed recall, mean ± SD	2.8 ± 1.4	2.9 ± 1.3	<0.001
Verbal fluency, mean ± SD	19.7 ± 7.5	20.1 ± 7.8	<0.001
Number of chronic conditions, n (%)			
Less than two chronic conditions	11585 (48)	35319 (64)	
More than two chronic conditions	12418 (52)	19953 (36)	<0.001
Countries, n (%)			
Austria	1425 (6)	3559 (6)	
Belgium	2047 (9)	4463 (8)	
Denmark	1227 (5)	3137 (6)	
France	1921 (8)	3666 (7)	
Germany	2194 (9)	4505 (8)	
Greece	492 (2)	2247 (4)	
Israel	742 (3)	1746 (3)	
Italy	1323 (6)	3814 (7)	
Netherlands	1186 (5)	3665 (7)	
Spain	1424 (6)	4393 (8)	
Sweden	1520 (6)	3687 (7)	
Switzerland	1006 (4)	2667 (5)	
Czech Republic	2060 (9)	4259 (8)	
Ireland	164 (1)	561 (1)	
Poland	637 (3)	1096 (2)	
Estonia	2176 (9)	2971 (5)	
Hungary	563 (2)	1282 (2)	
Portugal	414 (2)	832 (2)	
Slovenia	1107 (5)	1901 (3)	
Luxembourg	375 (2)	820 (1)	<0.001
Birth Cohort, n (%)			
After 1945	11675 (49)	29207 (53)	

Between 1939 and 1945	5210 (22)	11517 (21)	
Between 1929 and 1938	5242 (22)	10617 (19)	
Between 1919 and 1928	1876 (8)	3930 (7)	<0.001

Notes. Baseline = the first measurement occasion for each participant; SD = standard deviation; p values are based on the analysis of variance and chi-square tests for continuous and categorical variables, respectively, testing the effect of sleep quality at baseline (poor sleep vs. good sleep quality) on these variables.

Associations of sleep quality and physical activity with depressive symptoms

Table 2 and supplemental table S1 show the associations of sleep quality and physical activity with depressive symptoms. Relative to participants with good sleep quality, participants with poor sleep quality had a higher number of depressive symptoms (Model 1; b = 1.85, 95% confidence interval [95% CI] = 1.83 – 1.87, $p < .001$). This association remained significant in the fully adjusted model (Model 2; b = 1.78, 95% CI = 1.77 – 1.81, $p < .001$). Compared with physically active participants, physically inactive participants exhibited a higher number of depressive symptoms (Model 1; b = 0.44, 95% CI = 0.43– 0.46, $p < .001$). This association remained significant in the fully adjusted model (Model 2; b = 0.32, 95% CI = 0.30 – 0.33, $p < .001$).

Table 2. Coefficients of sleep, physical activity, and their interaction effect on the number of depressive symptoms

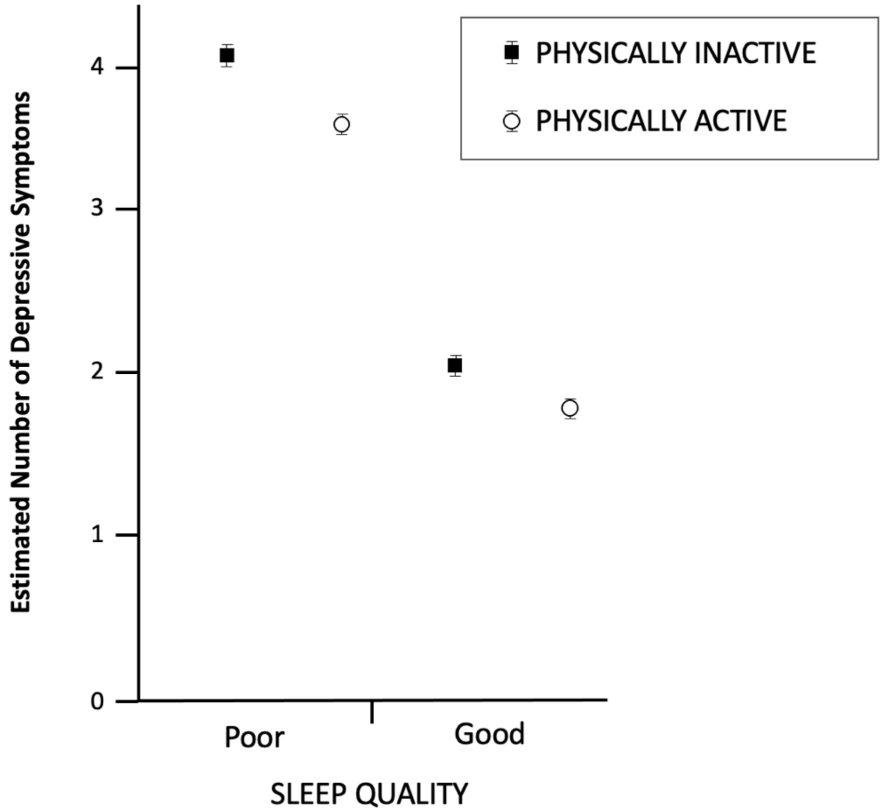
Depressive symptoms								
	Model 1 (no interaction term)				**Model 2** (includes the interaction term)			
Exposures	Minimally adjusted		Fully adjusted		Minimally adjusted		Fully adjusted	
	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*
Intercept	1.22 (1.20; 1.24)	<.001	1.77 (1.72; 1.82)	<.001	1.24 (1.22; 1.26)	<.001	1.78 (1.73; 1.83)	<.001
Sleep quality (ref. good sleep quality)								
Poor sleep quality	1.85 (1.83; 1.86)	<.001	1.78 (1.77; 1.81)	<.001	1.80 (1.78; 1.82)	<.001	1.74 (1.72; 1.76)	<.001
Physical activity (ref. physically active)								
Physically inactive	0.44 (0.42;0.45)	<.001	0.32 (0.30;0.33)	<.001	0.38 (0.37;0.40)	<.001	0.27 (0.25;0.29)	<.001
Sleep quality × Physical activity								
Poor sleep × Physically inactive					0.17 (0.13; 0.20)	<.001	0.15 (0.12; 0.19)	<.001

Notes. Minimally adjusted models are adjusted for wave of measurement, age, and sex. Fully adjusted models are further adjusted for body mass index, education, satisfaction with household income, cognitive functions, birth cohort, country of residence, attrition, and number of chronic diseases; 95% CI = 95% confidence interval.

Interaction between sleep quality and physical activity

Table 2, Figure 1, and supplemental table S1 show the interaction between the sleep quality and physical activity. The association between sleep quality and depressive symptoms was moderated by physical activity, as indicated by a significant interaction between sleep quality and physical activity (Model 2, minimally adjusted; b = 0.17, 95% CI = 0.13– 0.20, $p < .001$). This interaction remained significant in the fully adjusted model (Model 2, fully adjusted: b = 0.15, 95% CI = 0.12 – 0.19, $p < .001$). When sleep quality was poor, physically inactive participants had more depressive symptoms (b of the intercept = 3.94, CI = 3.89 – 4.0, $p < .001$) than physically active participants (b = 3.52, CI = 3.47 – 3.57, $p < .001$). Similarly, but to a lower extent, when sleep quality was good, physically inactive individuals had more depressive symptoms (b = 2.05, CI = 1.99 – 2.1, $p < .001$) than physically active participants (b = 1.78, CI = 1.73 – 1.83, $p < .001$).

Figure 1. Estimated number of depressive symptoms as a function of sleep quality and physical activity



Notes. b values of the intercept representing the estimated number of depressive symptoms according to the EURO-D scale and their 95% confidence interval are based on the fully adjusted model including the interaction term between sleep quality and physical activity (Model 2). Specifically, this model was adjusted for wave of measurement, age, sex, body mass index, education, satisfaction with household income, cognitive functions, birth cohort, country of residence, attrition, and number of chronic diseases.

Sensitivity and robustness analyses

The sensitivity analyses (supplemental table S2 and S3) yielded similar results to those of the main analyses. Specifically, poorer sleep quality and physical inactivity were both associated with a higher number of depressive symptoms. Moreover, the detrimental association between poor sleep quality and depressive symptoms was more pronounced in physically inactive individuals. Results of the first robustness analysis (Table S4), in which we introduced a time lag between the exposures and the outcome, confirmed that poor sleep quality and physical inactivity were both associated with the number of depressive symptoms. However, this analysis did not find evidence of an interaction between sleep quality and physical activity. Results of the second and third robustness analyses yielded similar results to those of the main analyses (Table S5 and S6).

Discussion

Main findings

To the best of our knowledge, our analysis of an existing large-scale longitudinal study,[32] is the first one to investigate the association of both sleep quality and physical activity with depressive symptoms and their potential interaction in adults 50 years of age or older. Our results showed that both poor sleep quality and physical inactivity were associated with an increased number of depressive symptoms. Further, we found evidence for an interaction between sleep quality and physical activity. Specifically, the negative association between sleep quality and depressive symptoms was amplified by physical inactivity. Hence, our study lends additional support to the synergistic effect of these two lifestyle behaviors on health outcomes, and demonstrates, for the first time, that this effect can be observed on a mental health outcome in adults 50 years or older. Two sensitivity and three robustness analyses confirmed the results of the main analysis, although one of the robustness analyses only confirmed the independent associations.

Comparisons with other studies

Our findings showing that poorer sleep quality was associated with higher levels of depressive symptoms is in line with the literature.[18,20,21,25,26] The mechanisms underlying the effect of poor sleep quality on depressive symptoms are still unclear, but several explanations have been put forward.[21,48] For example, poor sleep quality may contribute to increase the inflammation.[49] In turn, this inflammatory response may increase depressive symptoms.[50-52] Moreover, depression has been associated with the alteration of rapid eye movements during sleep,[53] a disruption accompanied with a decrease in monoamines (e.g., serotonin, norepinephrine, and dopamine),[54] which can in turn favor depression according to the “monoamine hypothesis”.[55] ~~[48,56]~~ Additional mechanisms, such as genetic factors influencing sleep and depression,[57-59] a detrimental influence of poor sleep quality on the regulation of emotions,[60-62] and a disruption of the circadian rhythm, which plays a key role in the sleep-wake regulation, have also been suggested to explain the link between poor sleep quality and depressive symptoms.[62,63]

The association between physical inactivity and increased levels of depressive symptoms is consistent with the literature.[16,17,22-24] Multiple pathways explaining the detrimental association between physical inactivity and depressive symptoms have been suggested.[64] For example, engaging in physical activity has been found to elicit neuroplastic mechanisms that could be protective against depression, such as an increased volume of the hippocampus and cortical regions,[65-68] a better white-matter integrity,[69,70] an improved cerebral flow,[71,72] and an increased circulation of neurotrophic factors, such as the brain-derived neurotrophic factor or the insulin growth factor-1.[73,74] Furthermore, being physically active reduces inflammation, as indexed by reduced levels of several circulating inflammatory factors.[75-77] Physical activity is also associated with a reduction in markers of oxidative stress,[78,79] which has been found to contribute to the development of depressive symptoms.[80] Finally, psychosocial mechanisms including higher self-esteem, social support, and self-efficacy have been proposed to explain the protective effect of physical activity on depression.[81-86]

Results suggesting an interaction effect between sleep quality and physical activity on depressive symptoms are consistent with previous studies investigating other health-related outcomes (e.g., cardiovascular disease, type 2 diabetes) and all-cause, cardiovascular disease, and cancer mortality.[30,31,87-89] For example, based on data from the UK Biobank cohort, Cassidy et *al.* showed that people with cardiovascular diseases and type 2 diabetes were more likely to be both physically inactive and to report poor sleep quality.[88] Similarly, based on data from a large-scale Taiwanese cohort, Chen et *al.* showed that short sleep duration, was associated with an increased mortality in physically inactive individuals, but not in physically active individuals.[87] Note that studies typically observed an inverted U relationships between sleep duration and risk of mortality, explaining why both short and long sleep durations are considered a risk factor.[90] Likewise, based on data from the UK Biobank cohort, Huang et *al.* showed that individuals combining poor sleep quality and low physical activity had higher risks of mortality, compared with individuals exhibiting good sleep quality and high physical activity.[31] Furthermore, results of this study showed that the detrimental effect of poor sleep quality on mortality risk was amplified by physically inactivity. To the best of our knowledge, the current study is the first one to demonstrate the interaction effect between physical inactivity and poor sleep quality on depressive symptoms.

Strengths and weaknesses

The strengths of the present study include a large sample size of non-institutionalized adults 50 years of age or older from different European countries and the use of a validated measure of depressive symptoms, the EURO-D scale.[34 35] However, our study also has some potential limitations. First, the correlational nature of our data cannot exclude reverse causality and thus prevents from inferring causal associations between sleep, physical activity, and depressive symptoms. To minimize the risk of reverse causation bias (i.e., due to a decline in physical activity levels and sleep quality in the preclinical phase of depression), we excluded participants with a suspicion of depression at baseline. To further reduce this reverse causation bias, we also conducted a robustness analysis that included a time lag between the exposures (sleep quality and physical activity) and the outcome (depressive symptoms). However, this analysis did not found evidence of an interaction between sleep quality and physical activity. Second, our measure of sleep relied on a single item that assessed whether participants had trouble sleeping, which prevents the possibility to investigate whether and how various aspects of sleep characteristic (e.g., sleep duration, quality, and timing) may have a potentially different effect on depressive symptoms. However, a single-item sleep-quality scale has proven to have good psychometrics features.[91] Third, we relied on a self-reported measure of physical activity based on two items. Although widely used in previous studies,[37-40 92-97] this measure may generate a misclassification bias between physically active and physically inactive individuals,[98] which may have distorted the associations observed in the current study. Moreover, this scale lacks granularity, thereby preventing the examination of how the various physical activity levels (e.g., light, moderate, vigorous) or types (e.g., occupation, transportation, household) may differently influence depressive symptoms.

Conclusion

Poor sleep quality and physical inactivity were both associated with an increased number of depressive symptoms. Further, the detrimental association between poor sleep quality and depressive symptoms was amplified in physically inactive participants. Our study highlights the need for developing interventions targeting both the promotion of good sleep quality and an active lifestyle to improve mental health in adults 50 years of age or older.

Author contributions: B.C.: conceptualization, writing – original draft; S.S.: data curation, writing – review & editing; S.M.: writing – review & editing; S.C.: supervision, writing – review & editing; D.S.: writing – review & editing; M.P.B.: supervision, writing – original draft.

Ethical approval: This study was part of the SHARE study, approved by the relevant research ethics committees in the participating countries.

Informed consent: All participants provided written informed consent.

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Data sharing: This SHARE dataset is available at http://www.share-project.org/data-access.html.

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Supplemental Material

Table S1. Results of Model 1 (without the interaction term) and Model 2 (including the interaction term between sleep quality and physical activity) with different levels of adjustment (minimally and fully adjusted).

Table S2. Results of the first sensitivity analysis excluding participants who dropped out during the survey.

Table S3. Results of the second sensitivity analysis excluding participants who died during the survey.

Table S4. Results of the first robustness analysis based on data with a time lag between the predictors and the outcome.

Table S5. Results of the second robustness analysis based on data in which the depressive symptoms scores did not include the item related to sleeping trouble.

Table S6. Results of the third robustness analysis based on data in which the depressive symptoms scores did not include the item related to sleeping trouble and in which participants who answered "one to three times a month" to either the moderate or the vigorous items were classified as physically active.

Table S1. Results of Model 1 (without the interaction term) and Model 2 (including the interaction term between sleep quality and physical activity) with different levels of adjustment (minimally and fully adjusted).

Depressive symptoms								
	Model 1				**Model 2**			
Exposures	Minimally adjusted		Fully adjusted		Minimally adjusted		Fully adjusted	
	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*
Intercept	1.22 (1.20; 1.24)	<.001	1.77 (1.72; 1.82)	<.001	1.24 (1.22; 1.26)	<.001	1.78 (1.73; 1.83)	<.001
Sleep quality (ref. good sleep quality)								
Poor sleep quality	1.85 (1.83; 1.87)	<.001	1.78 (1.77; 1.81)	<.001	1.80 (1.78; 1.82)	<.001	1.74 (1.72; 1.76)	<.001
Physical activity (ref. physically active)								
Physically inactive	0.44 (0.43;0.46)	<.001	0.32 (0.30;0.33)	<.001	0.38 (0.37;0.40)	<.001	0.27 (0.25;0.29)	<.001
Sleep quality × Physical activity								
Poor sleep × Physically inactive					0.17 (0.13; 0.20)	<.001	0.15 (0.12; 0.19)	<.001
Covariates								
Wave of measurement	0.06 (0.05; 0.06)	<.001	0.07 (0.07; 0.08)	<.001	0.06 (0.05; 0.06)	<.001	0.07 (0.07; 0.08)	<.001
Age (ref. 50-64)								
65-79	0.17 (0.15; 0.19)	<.001	-0.13 (-0.16; -0.10)	<.001	0.17 (0.15; 0.19)	<.001	-0.13 (-0.16; -0.10)	<.001
80-96	0.47 (0.43; 0.50)	<.001	-0.13 (-0.19; -0.08)	.056	0.47 (0.43; 0.50)	<.001	-0.32(-0.34; -0.30)	.056
Gender (ref. male)								
Female	-0.32 (-0.34; -0.30)	<.001	-0.32 (-0.34; -0.30)	<.001	-0.32 (-0.34; -0.30)	<.001	-0.32 (-0.34; -0.30)	<.001
Body mass index (ref. normal weight)								
Underweight			0.31 (0.24; 0.38)	<.001			0.31 (0.24; 0.39)	<.001
Overweight			-0.06 (-0.08; -0.05)	<.001			-0.07 (-0.08; -0.05)	<.001
Obese			-0.01 (-0.03; 0.01)	.404			-0.01 (-0.03; 0.01)	.371
Cognitive function								
Verbal fluency			-0.01 (-0.01; -0.01)	<.001			-0.01 (-0.01; -0.01)	<.001
Memory recall			-0.11 (-0.12; -0.10)	<.001			-0.11 (-0.12; -0.10)	<.001
Ability to make ends meet (ref. easily)								
Fairly easily			0.10 (0.08; 0.13)	<.001			0.11 (0.08; 0.13)	<.001
With some difficulty			0.33 (0.30; 0.35)	<.001			0.33 (0.30; 0.35)	<.001
With great difficulty			0.66 (0.62; 0.69)	<.001			0.66 (0.62; 0.69)	<.001
Education (ref. primary)								
Secondary			-0.03 (-0.05; -0.01)	.041			-0.03 (-0.05; -0.01)	.040
Tertiary			-0.01 (-0.03; 0.02)	.745			-0.01 (-0.03; 0.02)	.747
Chronic conditions (ref. less than two)								

Two or *more than two*			0.37 (0.36; 0.39)	<.001			0.37 (0.36; 0.39)	<.001
Birth cohorts (ref. After 1945)								
1919-1928			0.30 (0.25; 0.36)	<.001			0.30 (0.24; 0.36)	<.001
1929-1938			0.14 (0.10; 0.18)	<.001			0.14 (0.10; 0.18)	<.001
1939-1945			0.01 (-0.02; 0.40)	.399			0.02 (-0.02; 0.40)	.405
Countries (ref. Belgium)								
Austria			-0.20 (-0.25; -0.16)	<.001			-0.20 (-0.25; -0.16)	<.001
Denmark			-0.26 (-0.30; -0.21)	<.001			-0.26 (-0.30; -0.21)	<.001
France			0.18 (0.13; 0.22)	<.001			0.18 (0.13; 0.22)	<.001
Germany			-0.16 (-0.20; -0.12)	<.001			-0.16 (-0.20; -0.12)	<.001
Greece			-0.43 (-0.48; -0.38)	<.001			-0.43 (-0.48; -0.38)	<.001
Israel			-0.10 (-0.16; -0.05)	<.001			-0.10 (-0.16; -0.05)	<.001
Italy			0.01 (-0.01; 0.08)	.167			0.01 (-0.01; 0.08)	.152
Netherlands			-0.13 (-0.18; -0.09)	<.001			-0.13 (-0.18; -0.09)	<.001
Spain			-0.21 (-0.26; -0.17)	<.001			-0.21 (-0.26; -0.17)	<.001
Sweden			-0.11 (-0.16; -0.07)	<.001			-0.11 (-0.16; -0.07)	<.001
Switzerland			-0.13 (-0.17; -0.07)	<.001			-0.12 (-0.17; -0.07)	<.001
Czech Republic			-0.32 (-0.37; -0.29)	<.001			-0.33 (-0.37; -0.29)	<.001
Ireland			-0.34 (-0.44; -0.23)	<.001			-0.34 (-0.44; -0.23)	<.001
Poland			0.18 (0.12; 0.25)	<.001			0.18 (0.12; 0.24)	<.001
Estonia			0.17 (0.07; 0.16)	<.001			0.12 (0.07; 0.16)	<.001
Hungary			-0.22 (-0.29; -0.14)	<.001			-0.22 (-0.29; -0.14)	<.001
Portugal			0.01 (-0.02; 0.15)	.109			0.01 (-0.01; 0.15)	.095
Slovenia			-0.29 (-0.34; -0.23)	<.001			-0.29 (-0.34; -0.23)	<.001
Luxembourg			-0.10 (-0.19; -0.02)	.018			-0.10 (-0.19; -0.02)	.018

Note. Minimally adjusted models are adjusted for wave of measurement, age, and sex. Fully adjusted models are further adjusted for body mass index, education, satisfaction with household income, cognitive functions, birth cohort, country of residence, attrition, and number of chronic diseases. 95% CI = 95% confidence interval.

Table S2. Results of the first sensitivity analysis excluding participants who dropped out during the survey.

Depressive symptoms (N = 54,944)								
	Model 1				**Model 2**			
Exposures	Minimally adjusted		Fully adjusted		Minimally adjusted		Fully adjusted	
	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*
Intercept	1.24 (1.21; 1.27)	<.001	1.16 (1.11; 1.21)	<.001	1.27 (1.25; 1.30)	<.001	1.85 (1.79; 1.91)	<.001
Sleep quality (ref. good sleep quality)								
Poor sleep quality	1.86 (1.84; 1.88)	<.001	1.81 (1.79; 1.83)	<.001	1.80 (1.79; 1.83)	<.001	1.75 (1.73; 1.78)	<.001
Physical activity (ref. physically active)								
Physically inactive	0.46 (0.44;0.48)	<.001	0.37 (0.35;0.39)	<.001	0.40 (0.38;0.43)	<.001	0.28 (0.26;0.30)	<.001
Sleep quality × Physical activity								
Poor sleep × Physically inactive					0.18 (0.14; 0.22)	<.001	0.16 (0.12; 0.20)	<.001

Table S3. Results of the second sensitivity analysis excluding participants who died during the survey.

Depressive symptoms (N = 72,019)								
	Model 1				**Model 2**			
Exposures	Minimally adjusted		Fully adjusted		Minimally adjusted		Fully adjusted	
	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*
Intercept	1.21 (1.18; 1.23)	<.001	1.16 (1.12; 1.20)	<.001	1.25 (1.23; 1.27)	<.001	1.74 (1.69; 1.80)	<.001
Sleep quality (ref. good sleep quality)								
Poor sleep quality	1.85 (1.83; 1.86)	<.001	1.79 (1.78; 1.80)	<.001	1.80 (1.78; 1.82)	<.001	1.74 (1.72; 1.76)	<.001
Physical activity (ref. physically active)								
Physically inactive	0.38 (0.36;0.40)	<.001	0.30 (0.29;0.32)	<.001	0.33 (0.31;0.35)	<.001	0.22 (0.20;0.25)	<.001
Sleep quality × Physical activity								
Poor sleep × Physically inactive					0.17 (0.13; 0.20)	<.001	0.15 (0.12; 0.19)	<.001

Table S4. Results of the first robustness analysis based on data in which a time lag have been introduced between the predictors and the outcome.

Depressive symptoms (N = 51,024)								
	Model 1				**Model 2**			
Exposures	Minimally adjusted		Fully adjusted		Minimally adjusted		Fully adjusted	
	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*
Intercept	2.11 (2.07; 2.16)	<.001	2.76 (2.67; 2.84)	<.001	2.12 (2.07; 2.17)	<.001	2.77 (2.67; 2.85)	<.001
Sleep quality (ref. good sleep quality)								
Poor sleep quality	0.67 (0.64; 0.69)	<.001	0.60 (0.57; 0.63)	<.001	0.68 (0.62; 0.72)	<.001	0.57 (0.52; 0.63)	<.001
Physical activity (ref. physically active)								
Physically inactive	0.38 (0.35;0.40)	<.001	0.23 (0.20;0.26)	<.001	0.38 (0.34;0.41)	<.001	0.24 (0.21;0.27)	<.001
Sleep quality × Physical activity								
Poor sleep × Physically inactive					0.01 (-0.06; 0.06)	.921	0.03 (-0.09; 0.03)	.306

Table S5. Results of the second robustness analysis based on data in which the depressive symptoms scores did not include the item related to sleeping trouble.

Depressive symptoms (N = 79,274)								
	Model 1				**Model 2**			
Exposures	Minimally adjusted		Fully adjusted		Minimally adjusted		Fully adjusted	
	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*
Intercept	1.22 (1.20; 1.24)	<.001	1.77 (1.72; 1.82)	<.001	1.23 (1.22; 1.26)	<.001	1.78 (1.73; 1.83)	<.001
Sleep quality (ref. good sleep quality)								
Poor sleep quality	0.85 (0.83; 0.87)	<.001	0.78 (0.77; 0.80)	<.001	0.80 (0.78; 0.82)	<.001	0.74 (0.72; 0.76)	<.001
Physical activity (ref. physically active)								
Physically inactive	0.44 (0.43;0.46)	<.001	0.32 (0.30;0.33)	<.001	0.39 (0.37;0.41)	<.001	0.27 (0.25;0.29)	<.001
Sleep quality × Physical activity								
Poor sleep × Physically inactive					0.17 (0.13; 0.20)	<.001	0.15 (0.12; 0.19)	<.001

Table S6. Results of the third robustness analysis based on data in which the depressive symptoms scores did not include the item related to sleeping trouble and in which participants who answered "one to three times a month" to either the moderate or the vigorous items were classified as physically active.

Depressive symptoms (N = 79,274)								
	Model 1				**Model 2**			
Exposures	Minimally adjusted		Fully adjusted		Minimally adjusted		Fully adjusted	
	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*	b (95% CI)	*p*
Intercept	2.10 (2.07; 2.13)	<.001	2.41 (2.36; 2.47)	<.001	2.03 (1.99; 2.06)	<.001	2.34 (2.28; 2.40)	<.001
Sleep quality (ref. good sleep quality)								
Poor sleep quality	0.84 (0.83; 0.86)	<.001	0.78 (0.76; 0.80)	<.001	1.02 (0.97; 1.07)	<.001	0.97 (0.92; 1.01)	<.001
Physical activity (ref. physically active)								
Physically inactive	0.82 (0.80;0.84)	<.001	0.62 (0.59;0.65)	<.001	0.75 (0.71;0.77)	<.001	0.54 (0.51;0.57)	<.001
Sleep quality × Physical activity								
Poor sleep × Physically inactive					0.20 (0.15; 0.25)	<.001	0.21 (0.16; 0.26)	<.001