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

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ABSTRACT

Poor sleep quality and physical inactivity are known risk factors for depressive symptoms. Yet, whether these factors differently contribute to depressive symptoms and whether they interact with one another remains unclear. Here, we examined how sleep quality and physical activity influence depressive symptoms in 79,274 adults 50 years of age or older (52.4% women) from the Survey of Health, Aging and Retirement in Europe (SHARE) study. Sleep quality (poor vs. good), physical activity (inactive vs. active), and depressive symptoms (0 to 12 score) were repeatedly collected (7 waves of data collection) between 2004 and 2017. Results showed that sleep quality and physical activity were associated 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, compared to physically active participants, physically inactive participants reported more depressive symptoms (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 poor sleep quality and higher depressive symptoms was stronger in physically inactive than active participants. These findings suggest that, in adults 50 years of age or older, both poor sleep quality and physical inactivity are related to an increase in depressive symptoms. Moreover, the detrimental association between poor sleep quality and depressive symptoms is amplified in physically inactive individuals.

1. Introduction

Depression is a mental disorder affecting over 300 million people (World Health Organization, 2017a) and a leading cause of disability worldwide (Lépine and Briley, 2011). Depressive symptoms include persistent feeling of sadness, fatigue or loss of interest, diminished appetite, sleepiness, and worthlessness (Cotman et al., 2007; American Psychiatric Association A, 1980). These symptoms have a major impact on quality of life and daily functioning (Kessler, 2012), and their prevalence increases with age (Kok and Reynolds, 2017). Depression affects 7% of the world's older population (Luppa et al., 2012; World Health Organization, 2017b) and increases the risk for detrimental health-related outcomes in this population, including all-cause, cardiovascular, and stroke mortality (Lépine and Briley, 2011; Wei et al., 2019; Correll et al., 2017), coronary diseases (Wulsin and Singal, 2003; Gan et al., 2014), insulin resistance (Kan et al., 2013), and overweight (Lépine and Briley, 2011; Luppino et al., 2010). Moreover, depression is associated with cognitive and functional impairment, as well as social dysfunction (Chisholm et al., 2016). 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

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the development of depressive symptoms (Hsueh et al., 2021; Choi et al., 2019).

Poor sleep quality (i.e., individual's self-satisfaction with all aspect of the sleep experience) (Nelson et al., 2022)), inadequate sleep duration (i.e., shorter or longer sleep duration as compared to the 7–8 h of "normal" sleep) (Bin, 2016), and physical inactivity have been associated with negative health outcomes including depressive symptoms (Hsueh et al., 2021; Choi et al., 2019; Alvaro et al., 2013; Neckelmann et al., 2007; Baglioni et al., 2011; Schuch et al., 2018; Mammen and Faulkner, 2013; Rebar et al., 2015). 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 h per night (Li et al., 2017; Lin et al., 2021). Likewise, a recent study showed that older adults accumulating at least 3500 steps per day demonstrated a reduced risk of developing depressive symptoms, with 7000 steps per day providing the highest protective effect (Hsueh et al., 2021). 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 (Chastin et al., 2021; DiPietro et al., 2020). 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 h per night), which may represent an epiphenomenon of comorbidity (Stranges et al., 2008), was associated with an increased risk of mortality, but only among individuals reporting low usual levels of physical activity (Bellavia et al., 2014). 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 (Huang et al., 2021), although the association with all-cause mortality was not observed in another large-scale study (Chastin et al., 2021). To the best of our knowledge, however, no study has yet directly examined the potential interactive association between sleep quality and physical activity with depressive symptoms. Note that inadequate sleep duration and poor sleep quality are considered as distinct factors that may have independent and combined effects on health-related outcomes. In particular, although additional research is needed, it has been suggested that sleep duration could be more important to explain physical health outcomes, while sleep quality could be more relevant to explain mental health outcomes (Bin, 2016).

To address this knowledge gap, we analyzed data obtained by a large-scale longitudinal study to investigate the associations 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 (Bellavia et al., 2014; Huang et al., 2021), we hypothesized that the negative association between sleep quality and depressive symptoms is exacerbated by physical inactivity. Finally, both age and gender have been related to sleep quality, physical activity, and depressive symptoms. Older individuals and women typically reported poorer sleep quality, lower levels of physical activity, and higher depressive symptoms relative to younger individuals and men (Luppa et al., 2012; Bromet et al., 2011; van den Berg et al., 2009; van de Straat et al., 2020; Kessler and Bromet, 2013; Cheval et al., 2018; Lee, 2005; Reyner and Horne, 1995; Crowley, 2011). Moreover, the association between physical activity and sleep quality on depressive symptoms may depend on individuals' age or gender, though current evidence are still inconclusive (Fukukawa et al., 2004; Gadie et al., 2017; Addison-Brown et al., 2014; Schechtman et al., 1997; Carroll et al., 2010). Accordingly, to account for these potential differences, the present study examined whether the independent and combined associations of sleep quality and physical activity with depressive symptoms were patterned by age and gender.

2. Methods

2.1. Study design

The Survey of Health, Aging 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. Data collection was performed using computer-assisted personal interviewing to increase the standardization of the procedure and improve measurement reliability between participants. 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 (Börsch-Supan et al., 2013).

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 (Sabia et al., 2017), we excluded participants with a suspicion of depression at baseline as indicated by scores $\geq$4 on the EURO-D scale (Castro-Costa et al., 2008; Prince et al., 1999), Fig. 1 shows the flowchart.

2.2. Measures

2.2.1. Outcome: Depressive symptoms

Depressive symptoms were measured using the EURO-D scale using computer-assisted personal interviewing, 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 (Castro-Costa et al., 2008; Prince et al., 1999). Note that we conducted a robustness in which the depressive symptoms score was calculated without the item measuring sleep trouble (see robustness analysis section).

2.2.2. Predictors: Sleep quality and physical activity

Sleep quality, assessed using computer-assisted personal interviewing, 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 (van de Straat et al., 2020).

Physical Activity, assessed using computer-assisted personal interviewing, 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?" (Cheval et al., 2020; Cheval et al., 2019; de Souto et al., 2017). 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 (Cheval et al., 2018), this strategy reduces the potential misclassification bias that would lead physically inactive participants being incorrectly classified as physically active.

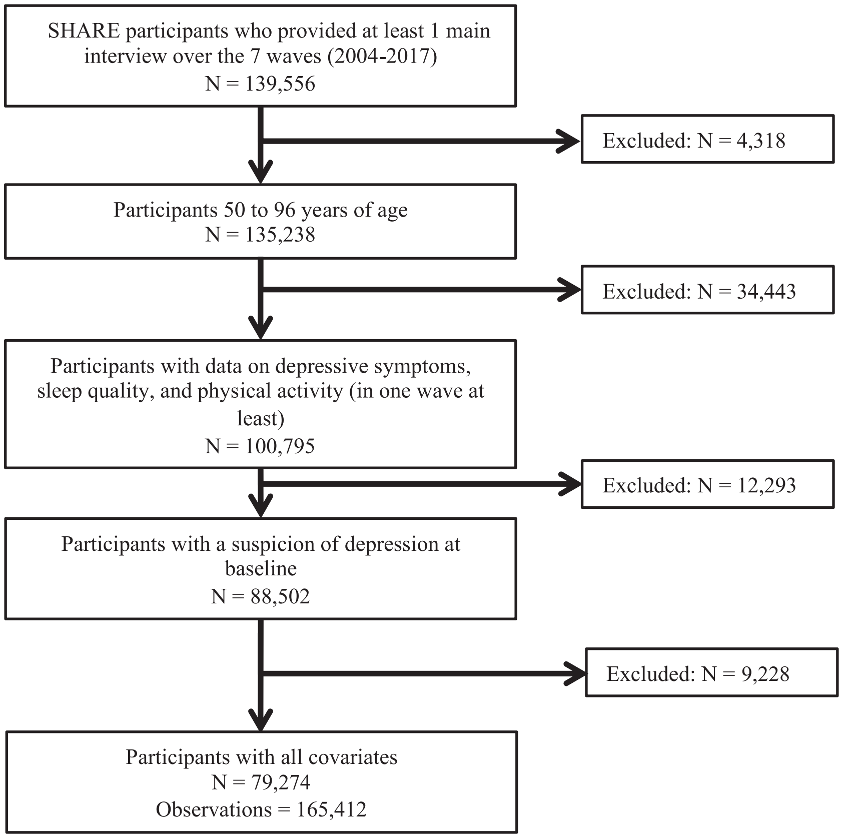

Fig. 1. Flowchart.

2.2.3. 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), *gender* (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) (United Nations Educational, 2006), *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).

2.3. Statistical analyses

All analyses were performed using R version 4.0.3 and were two-sided (Team RC. R Core Team. R, 2019). 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 (Bates et al., 2014; Kuznetsova et al., 2015). 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 (Boisgontier and Cheval, 2016). Moreover, participants with missing observations can be included as these models do not require an equal number of observations across participants (Raudenbush and Bryk, 2002).

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 gender 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. Statistical assumptions associated with linear mixed models, including normality of the residuals, linearity, multicollinearity (variance inflation factors), and undue influence (Cook's distances) were met.

2.3.1. 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.

Four 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 (Cheval et al., 2021), 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. Finally, the fourth robustness analysis was also based on the 11-item EURO-D scale but examined the lagged associations between the predictors and the outcome.

2.3.2. Exploratory analyses

We examined whether age group (50–64; 65–79; 80–96) and gender (man vs. woman) moderated the independent and combined associations of sleep quality and physical activity with depressive symptoms. To formally test these moderating patterns, we included interaction terms between age group (or gender), sleep quality, and physical activity. Significant interactions would indicate that the independent and/or combined associations were significantly moderated by age group and/or gender.

3. Results

3.1. 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* < 0.001).

3.2. 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, $p < .001$).

3.3. Interaction between sleep quality and physical activity

Table 2, Fig. 2, 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 poor sleep quality and physical inactivity (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

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	16,947 (71)	41,467 (75)	
Physically inactive	7051 (29)	13,804 (25)	<0.001
Other covariates			
Age, n (%)			
50–64	12,983 (54.1)	32,266 (58)	
65–79	9138 (38.1)	19,254 (35)	
80–96	1882 (7.8)	3751 (7)	<0.001
Gender, n (%)			
Women	15,239 (63)	26,362 (48)	
Men	8764 (37)	28,909 (52)	<0.001
Body mass index, n (%)			
Underweight	324 (1)	558 (1)	
Normal weight	8588 (36)	20,411 (37)	
Overweight	9629 (40)	23,601 (43)	
Obesity	5462 (23)	10,701 (19)	<0.001
Education, n (%)			
Primary	5572 (23)	12,285 (22)	
Secondary	13,541 (57)	30,262 (55)	
Tertiary	4890 (20)	12,724 (23)	<0.001
Ability to make ends meet			
With great difficulty, n (%)	2466 (10)	4495 (8)	
With some difficulty, n (%)	5376 (23)	10,896 (20)	
Fairly easily, n (%)	7447 (31)	17,348 (31)	
Easily, n (%)	8714 (36)	22,532 (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	11,585 (48)	35,319 (64)	
More than two chronic conditions	12,418 (52)	19,953 (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	11,675 (49)	29,207 (53)	
Between 1939 and 1945	5210 (22)	11,517 (21)	
Between 1929 and 1938	5242 (22)	10,617 (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 association of sleep quality at baseline (poor sleep vs. good sleep quality) with these variables.

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

Depressive symptoms								
	Model 1 (no interaction term)				Model 2 (includes the interaction term)			
Exposures	Minimally adjusted b (95% CI)	p	Fully adjusted b (95% CI)	p	Minimally adjusted b (95% CI)	p	Fully adjusted b (95% CI)	p
Intercept	1.22 (1.20; 1.24)	<0.001	1.77 (1.72; 1.82)	<0.001	1.24 (1.22; 1.26)	<0.001	1.78 (1.73; 1.83)	<0.001
Sleep quality (ref. good sleep quality)								
Poor sleep quality	1.85 (1.83; 1.86)	<0.001	1.78 (1.77; 1.81)	<0.001	1.80 (1.78; 1.82)	<0.001	1.74 (1.72; 1.76)	<0.001
Physical activity (ref. physically active)								
Physically inactive	0.44 (0.42;0.45)	<0.001	0.32 (0.30;0.33)	<0.001	0.38 (0.37;0.40)	<0.001	0.27 (0.25;0.29)	<0.001
Sleep quality × Physical activity								
Poor sleep × Physically inactive					0.17 (0.13; 0.20)	<0.001	0.15 (0.12; 0.19)	<0.001

Notes. Minimally adjusted models are adjusted for wave of measurement, age, and gender. 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.

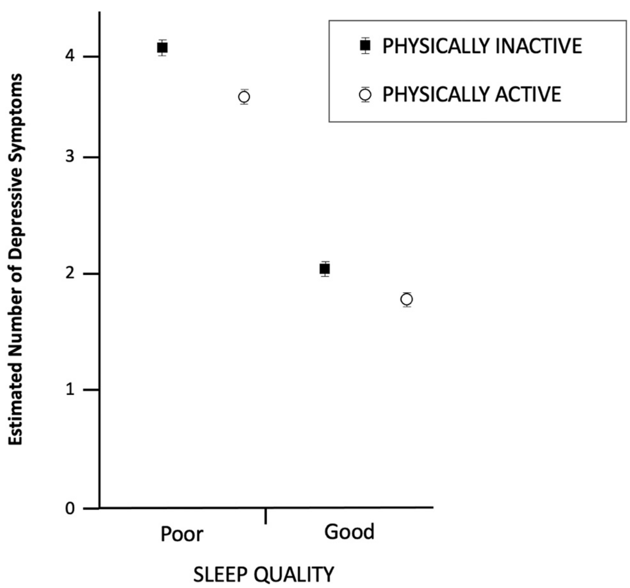

Fig. 2. Estimated number of depressive symptoms as a function of sleep quality and physical activity.
Notes. b values of the intercept representing the estimated number of depressive symptoms according to the EURO-D scale and their 95% confidence interval are based on the fully adjusted model including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

symptoms (b = 2.05, CI = 1.99–2.1, $p < .001$) than physically active participants (b = 1.78, CI = 1.73–1.83, $p < .001$).

3.4. Sensitivity and robustness analyses

The sensitivity analyses (supplemental Tables 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. A result also observed in the last robustness analysis (Table S7). Results of the second and third robustness analyses yielded similar results to those of the main analyses (Tables S5 and S6).

3.4.1. Exploratory analyses

3.4.1.1. Moderation by age group. Results testing whether age group moderated the pattern of the association showed that, compared to individuals aged 50–64 years, the association between poor sleep quality and depressive symptoms was less pronounced in individuals aged 65–49 years (b = −0.13, CI = −0.10 to −0.17, $p < .001$) and 80–96 years (b = −0.29, CI = −0.19 to −0.20, $p < .001$). In contrast, compared to individuals aged 50–64 years, the association between physical inactivity and more depressive symptoms was more pronounced in individuals aged 65–49 years (b = 0.16, CI = 0.12–0.21, $p < .001$) and 80–96 years (b = 0.30, CI = 0.22–0.38, $p < .001$). However, the interaction between poor sleep quality and physical inactivity was not significantly moderated by age group ($p = .310$ and $p = .311$, for the 65–49 and 80–96 year group, respectively) (Table S8).

3.4.1.2. Moderation by gender. Results testing whether gender moderated the pattern of the association showed that, compared to women, the association between physical inactivity and depressive symptoms was more pronounced in men (b = 0.05, CI = 0.01–0.09, $p = .023$). In contrast, although not significant, compared to women, the association between poor sleep quality and higher number of depressive symptoms was less pronounced in men (b = −0.03, CI = −0.07–0.01, $p < .001$). Finally, although not significant, compared to women, interaction between poor sleep quality and physical inactivity was more pronounced in men (b = 0.06, CI = −0.01–0.13, $p = .074$). The association between poor sleep quality and depressive symptoms in physically inactive individuals was more pronounced in men relative to women. Note that in the context of a very large sample size, these results need to be interpreted with caution (see discussion section) (Table S9).

4. Discussion

4.1. Main findings

To the best of our knowledge, our analysis of an existing large-scale longitudinal study (Börsch-Supan et al., 2013), 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. Exploratory analyses also revealed that these associations were moderated by age. The association between poor sleep quality and depressive symptoms was less pronounced in older participants, while the association between physical inactivity and depressive symptoms was more pronounced in older ages. Likewise, results showed that the latter association was more pronounced in men relative to women. 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. However, it should be noted that this interactive effect was not observed in the longitudinal analysis, highlighting the need to replicate this effect in other studies. Hence, our study lends additional support to the synergistic association of these two lifestyle behaviors on health outcomes, and demonstrates, for the first time, that this link 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.

4.2. 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 (Alvaro et al., 2013; Neckelmann et al., 2007; Baglioni et al., 2011; Li et al., 2017; Lin et al., 2021). The mechanisms underlying the association of poor sleep quality with depressive symptoms are still unclear, but several explanations have been put forward (Baglioni et al., 2011; Fang et al., 2019). For example, poor sleep quality may contribute to increase the inflammation (Irwin et al., 2006). In turn, this inflammatory response may increase depressive symptoms (Slavich and Irwin, 2014; Gimeno et al., 2009; Raison et al., 2013). Moreover, depression has been associated with the alteration of rapid eye movements during sleep (Adrien, 2002), a disruption accompanied with a decrease in monoamines (e.g., serotonin, norepinephrine, and dopamine) (Pace-Schott and Hobson, 2002), which can in turn favor depression according to the "monoamine hypothesis" (Hirschfeld, 2000; Fang et al., 2019; Krishnan and Nestler, 2008). Additional mechanisms, such as genetic factors influencing sleep and depression (Barclay and Gregory, 2013; Stein et al., 2018; Lind et al., 2017), a detrimental influence of poor sleep quality on the regulation of emotions (Koffel and Watson, 2009; Baglioni et al., 2010; Riemann et al., 2010), 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 (Riemann et al., 2010; Li et al., 2013).

The association between physical inactivity and increased levels of depressive symptoms is consistent with the literature (Hsueh et al., 2021; Choi et al., 2019; Schuch et al., 2018; Mammen and Faulkner, 2013; Rebar et al., 2015). Multiple pathways explaining the detrimental association between physical inactivity and depressive symptoms have been suggested (Kandola et al., 2019). 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 (Firth et al., 2018; Zheng et al., 2019; Colcombe et al., 2006; Ruscheweyh et al., 2011), a better white-matter integrity (Sexton et al., 2016; Zhu et al., 2015), an improved cerebral flow (Maass et al., 2015; Pereira et al., 2007), and an increased circulation of neurotrophic factors, such as the brain-derived neurotrophic factor or the insulin growth factor-1 (Huang et al., 2014; Ploughman et al., 2005). Furthermore, being physically active reduces inflammation, as indexed by reduced levels of several circulating inflammatory factors (Fedewa et al., 2017; Lin et al., 2015; Hamer et al., 2012). Physical activity is also associated with a reduction in markers of oxidative stress (de Sousa et al., 2017; Schuch et al., 2014), which has been found to contribute to the development of depressive symptoms (Black et al., 2015). Finally, psychosocial mechanisms including higher self-esteem, social support, and self-efficacy have been proposed to explain the protective association between physical activity and depression (Legrand, 2014; Hallgren et al., 2017; Harvey et al., 2010; Pickett et al., 2012; Wipfli et al., 2011; Knapen et al., 2005).

Results suggesting an interaction association 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 (Bellavia et al., 2014; Huang et al., 2021; Chen et al., 2021; Cassidy et al., 2016; Rayward et al., 2017). 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 (Cassidy et al., 2016). 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 (Chen et al., 2021). 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 (Cappuccio et al., 2010). 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 (Huang et al., 2021). Furthermore, results of this study showed that the detrimental association 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 this interaction between physical inactivity and poor sleep quality on depressive symptoms.

Age, birth cohort, gender, body mass index, cognitive function, economical condition, educational level, chronic condition, and countries were all significantly associated with depressive symptoms. These results were expected since previous literature has robustly demonstrated how demographic, socio-economic, and health-related factors are related to depressive symptoms. For example, older age, being a woman, having a higher body mass index, a disadvantaged socioeconomic status, chronic conditions, and weaker cognitive functioning have been related to an increased number of depressive symptoms (Kessler and Bromet, 2013; Fukukawa et al., 2004; Cheval et al., 2021; von Arx et al., 2019; Richardson et al., 2015; Nouwen et al., 2010; Pruchno et al., 2016; Aichele et al., 2018a; Aichele et al., 2018b; De Wit et al., 2009; Noh et al., 2015). Crucially, the independent and interactive associations between poor sleep quality and physical inactivity with depressive symptoms were only slightly attenuated after adjustment for those factors. This result supports the idea that poor sleep quality and physical inactivity are independent risk factors for depressive symptoms, above and beyond well-established risk factors of depression. Nevertheless, it should be acknowledged that controlling for extraneous factors is a very difficult task in observational designs. Randomized controlled trials offer a stricter control of extraneous factors and are thus needed to provide stronger evidence of the causal effect of sleep quality and physical activity on depressive symptoms.

Finally, exploratory analyses revealed that age, and to a lesser extent gender, moderated the association between sleep quality and physical activity on depressive symptoms. For example, results suggested that the strength of the association between poor sleep quality and depressive symptoms decreased with age, whereas the strength of the association between physical inactivity and depressive symptoms increased with age. The latter result is consistent with a study showing a protective effect of daily walking on depressive symptoms in older adults (65–75 years of age), but not in middle-age adults (40–64 years of age) (Fukukawa et al., 2004). Likewise, the results of the exploratory analyses draw attention to the fact that the independent and interactive associations of sleep quality and physical activity with depressive symptoms can be moderated by gender – the independent associations with depressive symptoms were weaker in men relative to women for sleep quality ($p = .079$) and stronger in men for physical inactivity ($p = .023$). Finally, the interactive associations ($p = .074$) were descriptively more pronounced in men relative to women, although not statistically significant. These exploratory results need to be interpreted with caution as, for gender, the associations exhibited p values above 0.02, providing rather weak evidence in the context of a very large sample size (Aichele et al., 2018b). Nevertheless, these analyses have the merit of highlighting the need to examine whether and how the association between sleep quality and depressive symptoms is patterned by age and gender. Future studies examining sleep and physical activity in relation to mental health should thus systematically test whether the observed associations are moderated by gender and age.

4.3. 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.(Castro-Costa et al., 2008; Prince et al., 1999). However, our study also has some potential limitations. First, the recruitment procedure occurs at age 50 years and older. As a result, respondents are more likely to be healthier than nonrespondents (Chalabaev et al., 2022). Moreover, attrition is more likely in individuals having poorer health at baseline or developing poorer health during the study (e.g., individuals who experienced an onset of depression). By including individuals with a single wave of measurement, our statistical approach minimized this bias. Likewise, our sensitivity analyses excluding participants who dropped out and died allowed to evaluate to what extent the main findings were robust and unlikely to be explained by the presence of individuals in poorer health condition only. Nevertheless, it is important to acknowledge that, although reduced, these selection biases are still present and that randomized controlled trials will be needed to provide a better control over extraneous factors. Second, 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 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 provide evidence of an interaction between sleep quality and physical activity. This finding discrepancy may be explained by the fact that 36% of cases were excluded in the lagged analyses (79,374 vs. 51,024 participants), which required data from at least two consecutive waves of measurement to be included in the study. Accordingly, the lagged analyses not only reduced the sample size, but could also have strengthened the selection bias – participants who maintained their commitment to the study could be healthier than the other respondents (Gray et al., 1996). However, lagged models respect the temporal precedence of exposure over outcome, which is an important criterion in assessing causality (Hill, 1965). Accordingly, beyond selection bias considerations, this result may question the validity of the interactive association between sleep quality and physical activity on depressive symptoms observed in the main analysis. In any case, the current observational data cannot provide conclusive evidence of a causal associations. Randomized controlled trials should be conducted to disentangle the complex associations, thought to be bidirectional (Chevance et al., 2022), occurring between these variables. Third, the measure of sleep relied on a single item that assessed whether participants had trouble sleeping, which precludes studying whether and how various aspects of sleep characteristic (e.g., sleep duration, quality, and timing) have different effects on depressive symptoms. However, a single-item sleep-quality scale has proven to have good psychometrics features (Snyder et al., 2018). Another limitation is the binary nature of the response, with participants classified as having a poor or good sleep quality, which lacks granularity. Similarly, the question included the notion of "recent change in pattern", which might have confused participants who experienced poor sleep quality for several years. Thus, the current findings need to be confirmed using more complete measures of sleep quality and/or using devices-based measures of sleep parameters (Cheval et al., 2022). Fourth, we relied on a self-reported measure of physical activity based on two items. Although widely used in previous studies (Cheval et al., 2018; Cheval et al., 2020; Cheval et al., 2019; de Souto et al., 2017; Chalabaev et al., 2022; Boisgontier et al., 2020; Maltagliati et al., 2021; Bourassa et al., 2017; Leist et al., 2020; Lindwall et al., 2011), this measure may generate a misclassification bias between physically active and physically inactive individuals (Prince et al., 2008), 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.

5. 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.

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.

CRediT authorship contribution statement

Boris Cheval: Conceptualization, Writing – original draft. **Silvio Maltagliati:** Writing – review & editing. **Stefan Sieber:** Data curation, Writing – review & editing. **Stéphane Cullati:** Supervision, Writing – review & editing. **David Sander:** Writing – review & editing. **Matthieu P. Boisgontier:** Supervision, Writing – original draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data are available with SHARE

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2022.107233.

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