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Depressive symptoms, life satisfaction, and prevalence of sleep disturbances in the general population

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Abstract

Objectives: It appears that not only depression, but also low life satisfaction (LS) is related to sleep complaints in the general population. We evaluate whether the prevalence of sleep complaints attributable to depressed mood is greater among participants with low LS.

Setting, participants and outcome measures: analysis of cross-sectional data from 3,880 cohort members from the German Heinz Nixdorf Recall study (2006-2008) aged 51 to 81 years. Standard mood (Center for Epidemiological Studies Depression scale (CES-D) for Depressive symptoms and the German Health Survey satisfaction scale for Life satisfaction) and sleep quality (Pittsburgh Sleep Quality Index, PSQI) measures were conducted as part of the survey. Multiple imputation was used to deal with missing data in outcome, exposures or covariates. Relative excess risk for interaction (RERI) and its 95% confidence intervals (CIs) were estimated using adjusted prevalence odds ratios.

Results: We observed an association between depressed mood (5-units increase in CES-D score) (POR=1.7 [95%CI = 1.6 ; 1.8]) and sleep complaints and between low LS (unsatisfied vs. very satisfied) (POR=1.5 [1.1 ; 2.2]) and sleep complaints. Also, we observed a synergistic effect between lower level of LS (not very satisfied) and depressed mood (score ≥ 16) on prevalence of sleep disorders (RERI = 3.7 [-0.2 ; 7.1]). Furthermore, these findings were corroborated in sensitivity analysis done with the complete case dataset and in sex-specific analyses (RERI = 5.5 [-0.4 ; 11.3] and RERI = 2.4 [-2.5 ; 7.4] for men and women, respectively).

Conclusions: Both depressed mood and LS are notably associated with sleep quality and these relationships are best captured by considering their joint effects. Depression and LS need to be taken in consideration when analyzing sleep quality.

Strengths and limitations

- Strengths: this study draws its strength from its size and from the fact that it is a population-based sample, with well-defined health outcomes, and inclusion of an exhaustive list of relevant covariates.
- Limitations: our sample consisted of adults with a restricted age range (51 - 81 years) and as with any cross-sectional design, the directionality of the observed associations cannot be determined.

INTRODUCTION

Sleep is an important source of general health and well-being.[1] Sleep disturbances have been associated with health problems, including poor self-rated health, psychological conditions, chronic medical conditions, and mortality.[2] The prevalence of sleep disturbances in the population is dependent on its definition, and it ranges from 6% (clinical diagnosis of insomnia) to 48% (difficulties in initiating or maintaining sleep or early morning awakening).[3] Considering its high prevalence and association with health conditions, there is a need to investigate the factors associated with sleep disturbances in order to develop strategies to prevent or delay its onset.

The experience of depressive symptoms is an affective disorder in which the prevailing emotional mood of a person is negatively distorted or inappropriate to the circumstances and is sustained over a particular period of time.[4] Depressive symptoms are considered an important risk factor for insomnia and conversely, sleep disturbances are very common (60-80% prevalence) among depressed patients.[2] In patients with depressive symptoms, insomnia appears either previously (40%) or simultaneously (22%) with other symptoms.[5] Following the International Classification of Disease, tenth revision (ICD-X) definition, sleep disturbances are very clearly a symptom of depression, and do not precede it. However, sleep complaints are a predictor for depressive relapse if they are a residual symptom after remission.

High life satisfaction (LS), is a latent disposition that contributes to subjective well-being.[6] LS is a relatively stable component of subjective well-being and refers to cognitive judgments, that was shown to remain quite constant even over a longer period of time.[7;8] A review

revealed that psychological well-being, and not only the absence of mental illness, has an effect on all-cause morbidity and mortality.[9] In addition, LS is related to health predictors such as favorable self-reported health, social support, and positive health behaviors.[10] Psychosomatic studies have shown moderate correlations between life satisfaction (LS) and depressive symptoms, and support independency indicating that research on indicators of well-being adds a distinctive dimension to psychiatric research.[11]

While there are numerous studies associating depression with poor sleep quality (for a review see [12]), there have been fewer studies evaluating associations of well-being and sleep quality. Cross-sectional studies have shown that lower well-being is associated with lower sleep quality.[13-15] Additionally these associations appear to be independent of psychological stressors.[16] It would therefore appear that not only depression is associated with sleep quality, but also well-being, on its own, is associated with sleep quality in the general population. Previous research has shown that depressive symptoms, a transitional period of low mood (state), are associated with worse sleep quality. However, it has not yet been investigated whether well-being, which tends to be stable over time (trait), can alter that connection. Recent research has shown that the relationship of trait and state positive mood on sleep quality is best captured by considering the joint effects of both stable and unstable aspects of mood.[15]

Aims

This study focuses on the association between depressive symptoms and sleep disturbances and whether this association can be modified by LS. The current study aims to extend our understanding of the relationship between depressive symptoms and the presence of sleep

disturbances. In particular, using cross-sectional data from the Heinz Nixdorf Recall Study (2006-2008), we assessed the presence of an interaction between depression and LS on sleep quality, by studying whether the joint effect of exposure to both factors was greater than the sum of their independent effects. We hypothesized that: a) depressive symptoms would negatively relate to sleep quality; b) LS would be positively associated with sleep quality and c) LS would modulate the relation between depressive symptoms and sleep quality. While an explanation of this link cannot be advanced in the frame of a cross-sectional study it seems nevertheless justified to test the assumption that LS moderates this association, such that stronger associations of depressive symptoms with sleep quality are observed among adults with lower LS.

MATERIALS AND METHODS

Study population and study sample

Data were derived from the Heinz Nixdorf Recall (Risk Factors, Evaluation of Coronary Calcium and Lifestyle) Study: a cross-sectional analysis of participants in the follow-up survey when sleep quality and mood assessments took place. The design of the study has been previously described in detail.[17] Briefly, during the baseline examination between December 2000 and August 2003, a total of 4,814 subjects aged between 45 and 75 years were recruited from three adjacent cities in the German Ruhr Area: Essen, Bochum, Mülheim/Ruhr.[17;18] The baseline recruitment proportion was 56%.[19] All subjects were invited for re-examination in 2006-2008. Overall, 154 out of 4,814 subjects (3%) died before re-examination, 503 refused examination (10%) leading to a final 5-years follow-up group of 4,157 subjects (87%). Data collection at follow-up was done through standardized interviews, clinical examination, comprehensive laboratory tests and self-administered questionnaires. The Heinz Nixdorf Recall study was approved by the institutional local ethics committee and has therefore been performed in accordance with the ethical standards laid out in the 1964 Declaration of Helsinki and its later amendments. An internal and external quality management system was established according to industrial standard norms DIN ISO 9001:2000/2008. All participants gave written informed consent.

Outcome

Sleep quality and sleep disturbances in the past month were measured through the Pittsburgh sleep quality index (PSQI).[20] The 19 self-rated items are combined to form seven

component scores, each of which has a range of 0-3 points. A score of "0" indicates no difficulty, while a score of "3" indicates severe difficulties. The seven component scores are then added to yield one "global" score, with a range of 0-20 points, "0" indicating no difficulty and "20" indicating severe sleep disturbances. For the purposes of our study, we examined the PSQI global score, which was calculated using the algorithm outlined in Buysse et al.[20] A PSQI global score greater than 5 was classified as poor quality sleep.[20]

Major exposures

Depressive symptoms last week was assessed by self-administered questionnaire through the 15 items Center for Epidemiologic Studies Depression scale (CES-D 15).[21;22] We modified the CES-D scale by excluding the symptom "my sleep was restless" to remove the item's correlation with questions on sleep disturbances.[23] Thus, the scale had 14 items and a score range 0 to 42, with higher scores indicative of more symptomatology. A cut-off of 18 has been suggested for depressive symptoms screening in the German population.[24] Because of the removal of an item we considered various cutoffs for depressive symptoms (16 and 18).

LS was measured by self-administered questionnaire through the following question: "how satisfied are you with your personal life?" Answer categories were: very satisfied; usually satisfied; unsatisfied.[25;26] For analysis purposes we dichotomized this item in "very satisfied" vs. all other categories, because only 6% of the population was categorized as "unsatisfied". In our sample, CES-D score was only moderately associated with the 3 LS categories (ß=0.04, S.E. =0.001 for both crude and age and sex-adjusted).

Covariates

Covariates known to affect sleep quality (outcome), that were also associated with either depressive symptoms or LS (exposures of interest) were identified from the literature[12-16] and discussed prior to the analyses. Socio-demographic variables: age, sex and socioeconomic status were obtained at baseline. Education was used as a proxy for the socio-economic status, classified in years of formal education according to the "International Standard Classification of Education" combining school and vocational training. Four categories were defined with the highest category of 18 and more years of education (equivalent to a University degree), category 3 with 14 to 17 years, category 2 with 11 to 13 years and the lowest category of 10 and less years (equivalent to a basic school degree and no vocational training). Anthropometric measurements (weight and height, body mass index (BMI)=kg/m^2) and blood pressure were determined at the clinical examination. Lifestyle factors were determined through personal interview (alcohol consumption and smoking habits). Social support, physical activity and life events were determined in the standardized interview. Social support was characterized with the Berkman-Syme's Social Network Index.[27] The components of the index are weighted in an algorithm resulting in four categories (I: low, II: mid-low, III: mid-high, IV: high). Physical activity was assessed by asking participants about the kind and duration of exercise performed in the preceding month, whereby 'physically inactive' meant having performed no exercise at all.[28] In the self-administered questionnaire participants were asked to report whether any stressful life events had occurred in the past 6 months, to which they could answer yes or no. Self-rated health was assessed in the interview by one question ('How would you, referring to the last

twelve months, describe your overall health status?') on a 5-point Likert-scale ('very good', 'good', 'moderate', 'poor' and 'very poor').

Statistical Methods

The present study includes only the 3,880 participants at follow-up (89% of the follow-up participants) who filled in the questionnaire. We identified minimally sufficient adjustment sets using diagrams that represent the relations among the exposure, outcome, and other variables.[29] All previously mentioned covariates were considered potential adjustment variables for the relation of LS and depressive symptoms with sleep quality. The minimally sufficient adjustment set for the association of LS and sleep quality included age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, modified CES-D, social support, life events, and physical activity. The minimally sufficient adjustment set for the association of depressive symptoms and sleep quality included age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, LS, social support, life events, and physical activity (see Appendix1a and Appendix1b).

We used multivariable logistic regression to estimate PORs (prevalence odds ratio) that account for depressive symptoms and LS on sleep quality. Exposures were analyzed dichotomously (CES-D score ≥16 vs. < 16 and LS=very satisfied vs. not very satisfied) and continuously (depressive symptoms per 5 unit increase, previously reported as clinically relevant) or categorically (LS 3 categories).[30] 722 of 3,880 (19%) subjects had missing data for sleep quality, depressive symptoms, LS or covariates. To manage missing data we undertook multiple imputation, using the MI procedure in SAS. We generated an imputed

database containing 20 imputed versions using all relevant variables predicting missingness (PSQI score, life satisfaction, CES-D score, age, alcohol consumption, BMI, blood pressure, cholesterol level, life events, sport index score, sex, smoking status, SNI and education level). Regression results were combined using the MIANALYZE procedure in SAS. We explored the pattern of missing data and performed sensitivity analyses on complete cases. Furthermore, we studied the presence of interaction (relative excess risk due to interaction [RERI]) between depressive symptoms and LS by comparing the joint effects of exposure to both factors with the sum of their independent effects. The estimated RERI was calculated as follows:[31]

$$RERI = OR_{11} - OR_{10} - OR_{01} + 1$$

where OR_{11} denotes OR among those exposed to both factors (depressive symptoms and low LS). A RERI of 0 means no interaction, a RERI > 1 means interaction without monotonicity assumption for one exposure and a RERI > 2 means interaction even without monotonicity assumption for both exposures.[31;32] We performed several sensitivity analyses with the complete case dataset (N=3158). In the first sensitivity analysis, we assumed that both depressive symptoms and sleep quality are strongly sex-dependent, therefore we did sex-stratified interaction analysis to investigate sex-specific patterns. In the second analysis, a higher cut-off for the depression scale (CES-D) was chosen, in order to investigate the robustness of our results. In a third analysis, exposures were treated as continuous (depressive symptoms) or categorical (LS) variables. All analyses were performed using SAS 9.3. (SAS Inc., Cary, NC).

RESULTS

Sample characteristics

A total of 1,932 participants (50%) were classified in the "good sleep quality" group which consisted of 57% men with a mean age of 64.4 years (SD 7.5, 51 to 81 years). A total of 1,477 participants (38%) were classified in the “sleep disturbances” category which was 38% male with a mean age of 65.3 years (SD 7.6). A further 471 participants (12%) did not answer the PSQI questionnaire. Table 1 shows demographic and clinical characteristics of participants stratified by sleep quality. Most clinical risk factors (age, hypertension, BMI, cholesterol and physical activity) were not different between the index population of “good sleep quality” and the “sleep disturbed” subgroup. On the contrary, most socio-demographic and psychological variables, e.g. educational level, self-rated health, social network index, life events, depressive symptoms and LS, showed different prevalences between subgroups. Additionally, participants in the good sleep quality group were more often men, current or former smokers and consumed more alcohol.

Association of depressive symptoms and life satisfaction with sleep quality

Table 2 presents the POR estimates for sleep quality with depressive symptoms as a continuous variable (data are shown per 5 unit increments in CES-D scale) and LS as a categorical variable. Similar results were obtained with complete case analysis and multiple imputation, thus we report effect estimates from the multiple imputation analyses. For “depressive symptoms” there was a stronger association between depressive symptoms (higher scores in CES-D; 5-units increment) and sleep disturbances (POR = 1.7, 95%CI 1.6 ; 1.8). The results of the logistic regression indicate that participants reporting lower LS

(unsatisfied) had an increased prevalence of suffering from sleep disturbances compared with participants reporting higher LS (very satisfied) (POR =1.5, 95%CI 1.1 ; 2.2). The results of the logistic regression with depression and LS dichotomized are presented in supplementary table 1. The results indicate that participants with higher CES-D scores (depressive symptoms; scores ≥ 16) had an increased prevalence of suffering from sleep disturbances than non-depressed participants (POR = 4.8, 95%CI 3.6 ; 4.5). Participants reporting lower LS had an increased prevalence of suffering from sleep disturbances compared with participants reporting higher LS (POR =1.6, 95%CI 1.3 ; 1.8).

Interaction between LS and depressive symptoms on the prevalence of sleep disturbances

The combined effects of depressive symptoms and LS on sleep quality were greater than the sums of the separate estimated effects (table 3 and supplementary table 2). Multiple imputation and complete case analysis yielded very similar results, thus we report here results from multiple imputation. The RERI for depressive symptoms (score ≥ 16 in the CES-D scale) and LS was 3.7 (95%CI=-0.2 ; 7.1), which indicates that because of the interaction between depressive symptoms and LS, the POR is 3.7 times higher than expected from the addition of the separate effects of depressive symptoms and LS alone. Additionally, the multiplicative interaction of depressive symptoms and LS on sleep quality was ratio of PORs=1.5 (95% CI=0.6 ; 3.6). Results for complete case analysis were comparable and are presented in supplementary table 2.

Sensitivity analysis

Several sensitivity analyses in the complete case dataset were performed. Sex-stratified interaction analysis produced similar results (RERI = 2.4 [-2.5 ; 7.4] and RERI= 5.5 [-0.4 ; 11.3] for women and men respectively) (supplementary tables 3 and 4), but have to be interpreted with caution due to the small numbers of participants in some of the categories. Additive and multiplicative interactions obtained with a higher cut-off for the CES-D scale (scores ≥ 18) were RERI = 4.2 (95%CI=-1.9 ; 10.4) and ratio of PORs=1.4 (95%CI=0.4 ; 4.8), respectively. We repeated the interaction analysis with depressive symptoms considered continuously and LS in 3-categories. Additive and multiplicative interaction values were estimated for non-dichotomous exposure variables: CES-D score 0 to 42, per 5-unit increase and 3-categories LS. The results of this logistic regression indicate that participants with higher CES-D scores (score 15-20) had an increased prevalence of suffering from sleep disturbances than participants with lower scores (score 0-5) (POR = 1.9; 95%CI=1.6 ; 2.3). Participants more dissatisfied with life ("unsatisfied") had an increased prevalence of suffering from sleep disturbances compared with participants satisfied with life ("very satisfied") (POR = 1.5; 95%CI=0.6 ; 3.9). Moreover, the RERI for depressive symptoms and LS (assessed by comparing "very satisfied" with "unsatisfied" and a CES-D score of 0 to a score of 16) was 5.4 (95%CI=-10.0 ; 20.8) and the multiplicative interaction (ratio of PORs) was 1.0 (95%CI=0.9 ; 1.2) (data not shown).

DISCUSSION

Findings from the current study showed that both depressive symptoms and LS were notably associated with sleep quality, emphasizing the importance of both stable and dynamic features of mood on sleep patterns. In agreement with previous studies, we found a negative relation between sleep and depressive symptoms [12] and an overall positive relation between good sleep quality and LS.[13-16] Furthermore, our results suggested that these relationships were best captured by considering the joint effects of depressive symptoms and LS, with higher depressive symptoms associated with substantially worse sleep quality, especially among individuals with lower LS.

Depressive symptoms and LS were only moderately inversely related in our population. This confirms previous literature reporting that they are distinct constructs.[11;33] Sleep disturbances are part of the diagnostic criteria for depression in ICD-10 and DSM-IV; therefore it is not surprising that CES-D and PSQI scores are so strongly associated. A number of previous studies have shown that depressive symptoms are related to poorer sleep in the adult population with OR of 1.5 to 3.0 in most studies.[2;34] Our results showed a higher POR for depressive symptoms (4.8, 95%CI 3.6 ; 6.5), probably due to the relatively high cut-off chosen in this study. Additionally, the OR for LS was similar to those previously reported, between 1.8 and 2.1 (POR=1.6, 95%CI=1.3 ; 1.8). [35;36] Although in concordance with those findings, the present results extend them in several important ways. Most notably, our study examined interaction effects of LS and depressive symptoms on sleep quality.

Ong et al. examined a similar interaction, however only on the multiplicative scale [15] in which they showed that well-being interacts with negative reactivity on overall sleep quality.[15] These results were replicated on the multiplicative scale and expanded on the additive scale in our study. The multiplicative and additive interaction analyses both examined whether the relative detriment of depressive symptoms on sleep quality was the same across LS groups. We found that participants with depressive symptoms had much worse sleep quality if they belonged to the non-satisfied group than if they belonged to the satisfied group (multiplicative interaction POR = 1.5, 95%CI= 0.6 ; 3.6). However, from a public health perspective, additive interaction is the relevant one, as it can help determine which subgroups would benefit most from a given treatment, i.e. psychotherapy to improve depressive symptoms and thus sleep quality in those participants with low LS. The additive interaction (RERI=3.7, 95%CI=-0.2 ; 7.1) indicates that there is a synergistic effect between depressive symptoms and LS, which substantially increased the prevalence of worse sleep quality. Our study suggests that the depressive symptoms-sleep quality association was modified by LS level in both the multiplicative and additive interaction analyses.

This study draws its strength from its size and from the fact that it is a population-based sample with well-defined health outcomes and inclusion of an exhaustive list of relevant covariates. Nevertheless, our conclusions are limited by several factors. Our sample consisted of adults with a restricted age range (51 - 81 years) and as with any cross-sectional design, the directionality of the observed associations cannot be determined. Regarding the representability of this study population, it has been previously reported that high social class and good health status were overrepresented at baseline of the Heinz Nixdorf Recall Study [19]. Moreover, we used a modified version of the CES-D scale to measure depressive

symptoms. Because of this modification, we could not consider previously validated cut-offs for our population. Therefore, we ran sensitivity analyses with various cut-offs (16 and 18) in order to identify relevant changes. In the present study, we did not use sex-specific cut-offs to detect depressive symptoms as previously described in the literature.[37] However, it has been recently pointed out that for women in several depression tests (Beck Depression Inventory - II, Inventory of Depressive Symptoms - self-report and the Montgomery-Asberg Depression Rating Scale) a higher cut-off than for men, discriminates better between depressed and non-depressed. Yet, they also affirm that it is too early to recommend gender specific reference values for those tests and that previous studies have found no sex differences for depression scales.[38] Finally, outcome and predictors (sleep quality, depressive symptoms and LS) have been analyzed as dichotomous variables, though they were documented as continuous. Nevertheless, we ran sensitivity analyses with continuous (depressive symptoms) and categorical (LS) exposure variables in complete case analysis in order to identify relevant changes. Finally, the RECALL study was not powered for this research question; therefore some estimates are very imprecise.

These results extend the study of depressive symptoms and LS, sleep quality and suggest that the association between depressive symptoms and sleep quality is modified by LS. Understanding the predictors of poor sleep quality may have important implications for future health outcomes, such as development of chronic medical conditions associated with poor sleep quality.

Contributor statement: ASP, ND, SM, SD, SM, AS, HK, RE and AS contributed to the study design and data acquisition. AS supervised all aspects of the study's execution. MEL planned the analysis and undertook the primary analysis and wrote the first draft of the paper. All authors critically reviewed the paper and approved the submitted version.

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Table 1. Demographic and clinical characteristics of participants stratified by sleep quality.

Data are presented as n (%) unless otherwise stated.

			Sleep quality	
Variable		**Total**	**Good [a]**	**Poor [b]**
			(N = 1932)	**(N = 1477)**
Sex	Women: n (%)	1746	823 (42.6)	923 (62.5)
	Men: n (%)	1663	1109 (57.4)	554 (37.5)
Education	< 10 years: n (%)	324	140 (7.3)	184 (12.5)
	11 – 13 years: n (%)	1910	1005 (52.0)	905 (61.3)
	14 – 17 years: n (%)	791	531 (27.5)	260 (17.6)
	≥ 18 years: n (%)	384	256 (13.3)	128 (8.7)
Smoking	Never smoker: n (%)	1392	731 (39.0)	661 (46.7)
	Former smoker: n (%)	1343	809 (43.1)	534 (37.7)
	Current smoker: n (%)	558	337 (18.0)	221 (15.6)
Self-rated health	Very good: n (%)	164	137 (7.3)	27 (1.9)
	Good: n (%)	1314	922 (49.2)	392 (27.7)

			Sleep quality	
Variable		**Total**	**Good [a]**	**Poor [b]**
			(N = 1932)	**(N = 1477)**
	Fair: n (%)	1275	645 (34.4)	630 (44.5)
	Poor: n (%)	446	137 (7.3)	309 (21.8)
	Very poor: n (%)	93	35 (1.9)	58 (4.1)
Social network index	I (low): n (%)	856	443 (23.7)	413 (29.2)
	II: n (%)	1254	715 (38.2)	539 (38.1)
	III: n (%)	942	567 (30.3)	375 (26.5)
	IV (high): n (%)	232	145 (7.8)	87 (6.2)
Hypertension [c]	Yes: n (%)	1250	755 (40.4)	495 (35.1)
Physical activity	Active: n (%)	1504	816 (43.5)	688 (48.6)
Life events in last 6 months	Yes: n (%)	695	346 (18.2)	349 (24.1)
Depressed mood (CES-D ≥ 16) [d]	Yes: n (%)	294	58 (3.1)	236 (16.3)
Life satisfaction	Very satisfied: n (%)	1194	778 (41.2)	416 (28.9)
	Quite satisfied: n (%)	1943	1045 (55.4)	898 (62.3)

		Sleep quality	
Variable	**Total**	**Good [a] (N = 1932)**	**Poor [b] (N = 1477)**
Unsatisfied: n (%)	192	65 (3.4)	127 (8.8)
Depressed mood: mean (SD) [d]	3338	5.3 (4.4)	9.5 (6.7)
Age years: mean (SD)	3409	64.4 (7.5)	65.3 (7.6)
BMI (kg /m^2) : mean (SD)	3287	28.1 (4.6)	28.3 (5.1)
Total Cholesterol mg/ dL: median (Q1;Q3)	3274	226 (199; 254)	223 (199; 249)
HDL Cholesterol mg/dL: median (Q1;Q3)	3274	59 (49; 71)	57 (48; 69)
Alcohol consumption ml/week: mean (SD)	3306	70.2 (102.7)	57.8 (107.6)

PSQI=Pittsburgh sleep quality index, CES-D= center for epidemiological studies depression scale, BMI=body mass index, HDL=high density lipoprotein. [a] Good sleep quality: PSQI score ≤ 5. [b] Poor sleep quality: PSQI score > 5. [c] Participants on antihypertensive medication or with systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg were defined as hypertensive. [d] CES-D scale excludes the item “my sleep was restless

Table 2. Association of depressed mood and life satisfaction with sleep quality. PORs per 5 unit increment in CES-D scale (depressed mood).

		Complete case analysis		Multiple imputation	
Model	**Adjusted for:**	**N**	**POR (95%CI)**	**N**	**POR (95%CI)**
Depressed mood (score 0 – 42; unit increment=5)					
1	-	3338	2.0 (1.8 – 2.1)	3880	1.8 (1.7 – 1.9)
2	Age and sex	3338	1.9 (1.8 – 2.1)	3880	1.8 (1.6 – 1.9)
3	Fully adjusted [a]	3163	1.8 (1.7 – 2.0)	3880	1.7 (1.6 – 1.8)
Life satisfaction (very -, quite satisfied, unsatisfied)					
1	-	3329		3880	
	Very vs. unsatisfied		3.7 (2.6 – 5.0)		3.6 (2.6 – 4.9)
	Quite vs. unsatisfied		2.3 (1.7 – 3.1)		2.3 (1.7 – 3.1)
2	Age and sex	3329		3880	
	Very vs. unsatisfied		4.2 (3.0 –		4.2 (3.0 –

		Quite vs. unsatisfied		5.8)	5.7)
				2.4 (1.7 –	2.4 (1.7 –
				3.2)	3.3)
3	Fully adjusted [b]		3163		3880
		Very vs. unsatisfied		1.5 (1.0 –	1.5 (1.1 –
		Quite vs. unsatisfied		2.2)	2.2)
				1.2 (0.9 –	1.3 (0.9 –
				1.8)	1.8)

POR=prevalence odds ratio, CI=confidence interval.

[a] Fully adjusted: age, sex, alcohol consumption, BMI (body mass index), blood pressure, total cholesterol, life satisfaction, life events, physical activity, education years, smoking and social support

[b] Fully adjusted: age, sex, alcohol consumption, BMI (body mass index), blood pressure, total cholesterol, CES-D score (center for epidemiological studies depression scale), life events, physical activity, education years, smoking and social support

Table 3. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems (multiple imputation, N=3880)

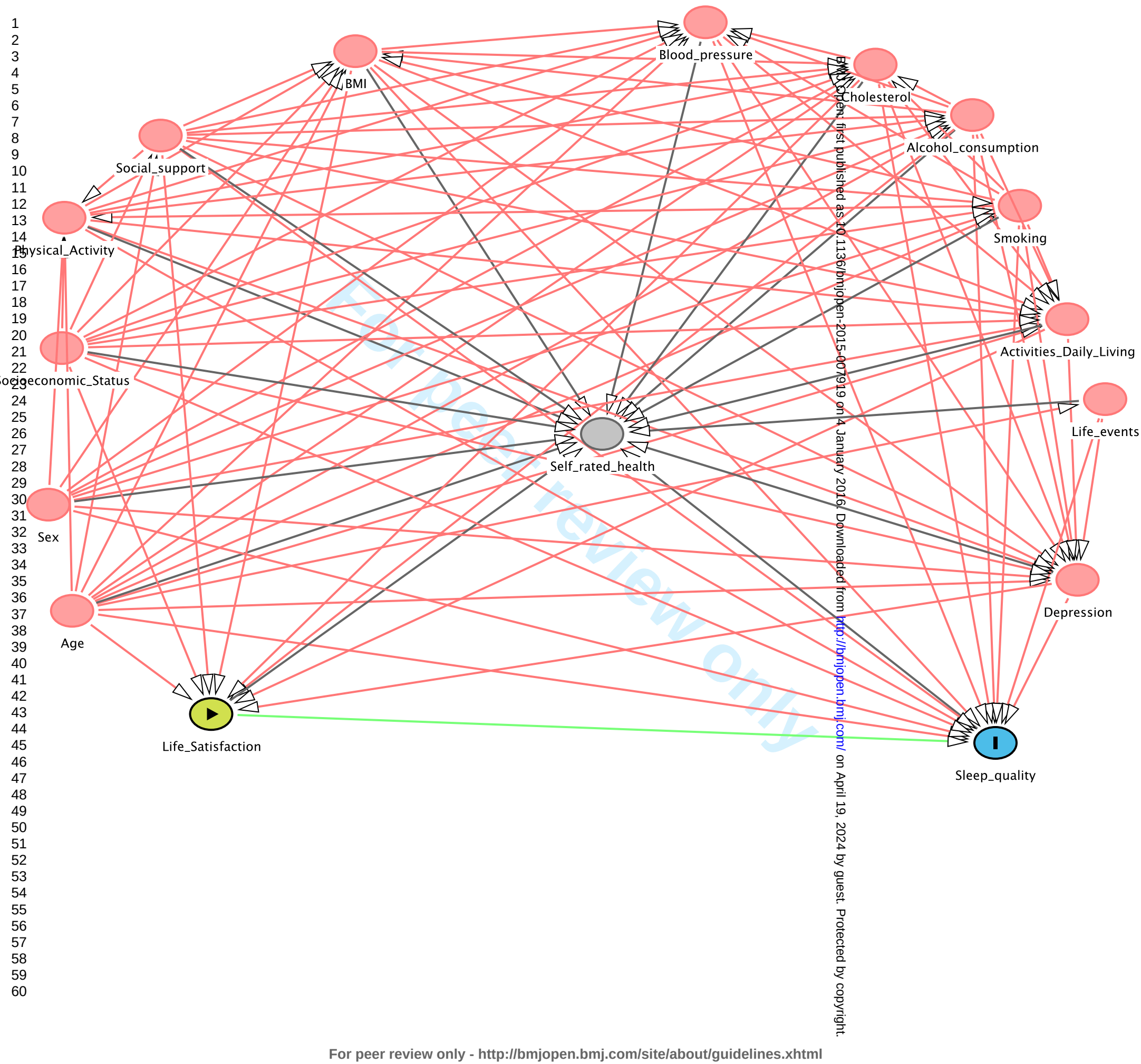
	Life satisfaction	
	very satisfied	not very satisfied
	POR (95% CI)	POR (95% CI)
Non-depressed mood (cut-off < 16)	1.0	1.5 (1.3 ; 1.8)
Depressed mood (cut-off ≥ 16)	3.4 (1.5 ; 7.9)	7.4 (3.5 ; 11.3)

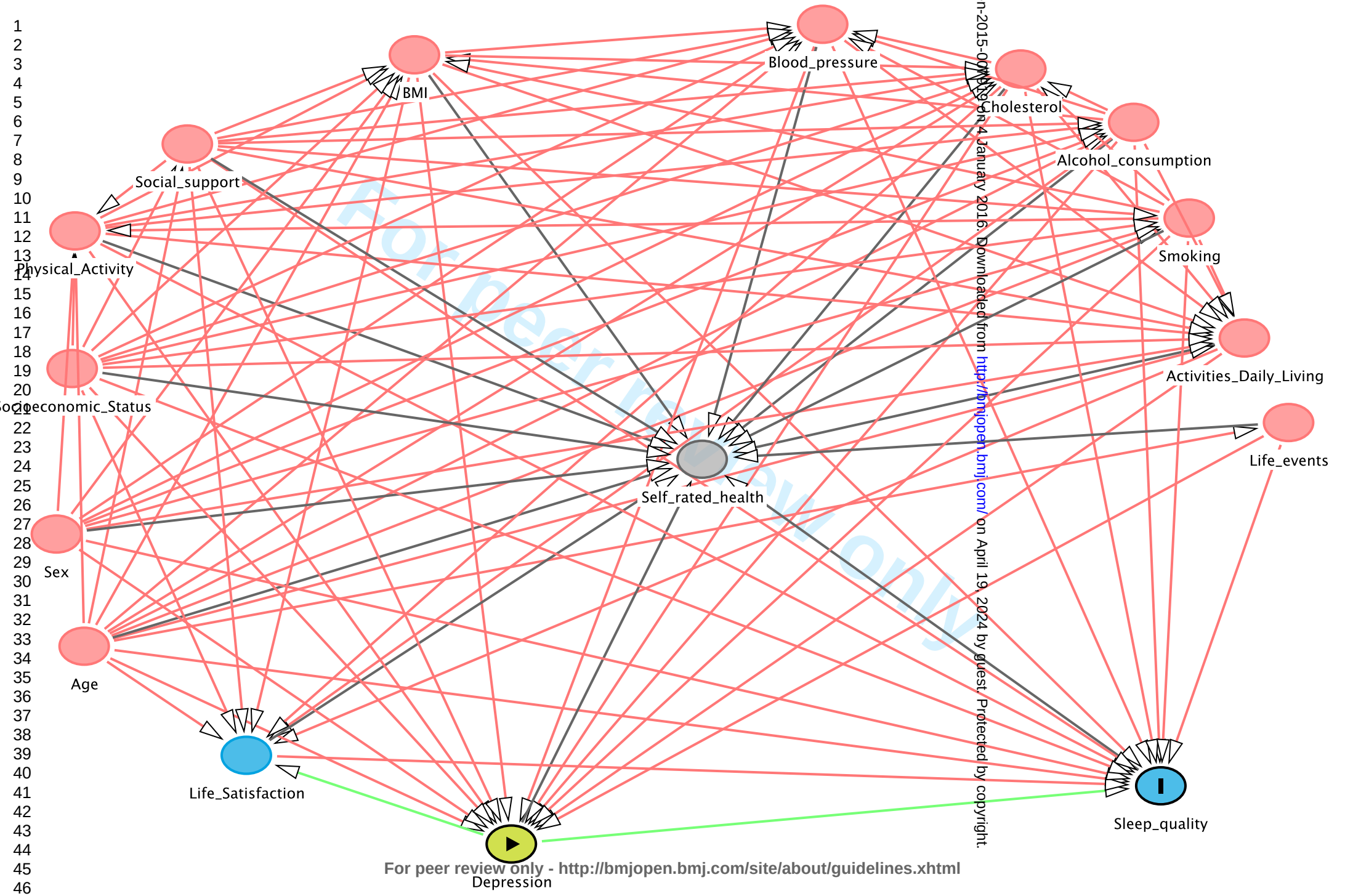
POR=prevalence odds ratio, CI=confidence interval.

Measure of interaction on additive scale: RERI (95% CI) = 3.7 (-0.2 ; 7.1)

Measure of interaction on multiplicative scale: ratio of PORs (95% CI) = 1.5 (0.6 ; 3.6)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.





Supplementary table 1. Association of depressed mood and life satisfaction with sleep quality.

		Complete case analysis		Multiple imputation	
Model	**Adjusted for:**	**N**	**POR (95%CI)**	**N**	**POR (95%CI)**
Depressed mood (<16 not depressed vs. ≥ 16 depressed mood (ref.))					
1	-	3338	6.2 (4.6 – 8.3)	3880	6.4 (4.8 – 8.5)
2	Age and sex	3338	5.8 (4.3 – 7.9)	3880	6.0 (4.5 – 8.0)
3	Age, sex, alcohol consumption, BMI, blood pressure, total cholesterol, life satisfaction, life events, physical activity, education years, smoking and social support	3158	4.6 (3.3 – 6.3)	3880	4.8 (3.6 – 4.5)
Life satisfaction (very satisfied vs. not very satisfied (ref.))					
1	-	3329	1.7 (1.5 – 2.0)	3880	1.7 (1.5 – 1.9)
2	Age and sex	3329	1.9 (1.6 – 2.2)	3880	1.9 (1.6 – 2.2)
3	Age, sex, alcohol consumption, BMI, blood pressure, total cholesterol, CES-D score, life events, physical activity, education years, smoking and social support	3158	1.6 (1.4 – 1.9)	3880	1.6 (1.3 – 1.8)

CES-D= center for epidemiological studies depression scale, BMI=body mass index, POR=prevalence odds ratio, CI=confidence interval.

Supplementary table 2. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems (N=3158)

	Life satisfaction				
	very satisfied		not very satisfied		**POR (95% CI) for life satisfaction within strata of depressed mood**
	N good sleep quality/ N poor sleep quality	POR (95% CI)	N good sleep quality/ N poor sleep quality	POR (95% CI)	
Non-depressed mood (cut-off < 16)	380 / 733	1.0	769 / 1011	1.6 (1.3 ; 1.8)	1.6 (1.3 ; 1.8)
Depressed mood (cut-off ≥ 16)	16 / 7	3.2 (1.3 ; 8.0)	195 / 47	7.3 (5.1 ; 10.4)	2.1 (0.8 ; 5.9)
POR (95% CI) for depressed mood within strata of LS		3.2 (1.3 ; 8.0)		4.7 (3.3 ; 6.6)	

Measure of interaction on additive scale: RERI (95% CI) = 3.6 (-0.2 ; 7.4)

Measure of interaction on multiplicative scale: ratio of PORs (95% CI) = 1.5 (0.6 ; 4.0)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

Supplementary table 3. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems for women (N=1604)

	Life satisfaction				**POR (95% CI) for life satisfaction within strata of depressed mood**
	very satisfied		not very satisfied		
	N sleep problems / no sleep problems	POR (95% CI)	N sleep problems / no sleep problems	POR (95% CI)	
Non-depressed mood (cut-off < 16)	248 / 337	1.0	450 / 396	1.6 (1.3 ; 2.0)	1.6 (1.3 ; 2.0)
Depressed mood (cut-off ≥ 16)	13 / 4	3.6 (1.1 ; 11.3)	130 / 26	6.6 (4.1 ; 10.5)	1.8 (0.4 ; 7.5)
POR (95% CI) for depressed mood within strata of LS		3.6 (1.1 ; 11.3)		4.2 (2.7 ; 6.7)	

Measure of interaction on additive scale: RERI (95% CI) = 2.4 (-2.5 ; 7.4)

Measure of interaction on multiplicative scale: ratio of PORs (95% CI) = 1.2 (0.3 ; 4.0)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

Supplementary table 4. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems for men (N=1554)

	Life satisfaction				**POR (95% CI) for life satisfaction within strata of depressed mood**
	very satisfied		not very satisfied		
	N sleep problems / no sleep problems	POR (95% CI)	N sleep problems / no sleep problems	POR (95% CI)	
Non-depressed mood (cut-off < 16)	132 / 396	1.0	319 / 615	1.5 (1.2 ; 2.0)	1.5 (1.2 ; 2.0)
Depressed mood (cut-off ≥ 16)	3 / 3	2.4 (0.5 ; 12.4)	65 / 21	8.4 (4.9 ; 14.5)	5.5 (0.6 ; 47.5)
POR (95% CI) for depressed mood within strata of LS		2.4 (0.5 ; 12.4)		5.4 (3.2 ; 9.1)	

Measure of interaction on additive scale: RERI (95% CI) = 5.5 (-0.4 ; 11.3)

Measure of interaction on multiplicative scale: ratio of PORs (95% CI) = 2.3 (0.4 ; 12.6)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Depressive symptoms, life satisfaction, and prevalence of sleep disturbances in the general population of Germany. Results from the Heinz Nixdorf Recall Study.

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Secondary Subject Heading:	Epidemiology, Geriatric medicine
Keywords:	depressed mood, life satisfaction, sleep quality, interaction

Depressive symptoms, life satisfaction, and prevalence of sleep disturbances in the general population of Germany. Results from the Heinz Nixdorf Recall Study.

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Running head: depression and life satisfaction synergy on sleep

Keywords: depressive symptoms, life satisfaction, sleep quality, interaction

Word count: 46 references, 3726 main text, 3 tables, 4 supplementary tables

Abstract

Objectives: It appears that not only depression, but also low life satisfaction (LS) is related to sleep complaints in the general population. We evaluate whether the prevalence of sleep complaints attributable to depressed mood is greater among participants with low LS.

Setting, participants and outcome measures: Analysis of cross-sectional data from 3,880 cohort members from the German Heinz Nixdorf Recall study (2006-2008) aged 51 to 81 years. Standard mood (Center for Epidemiological Studies Depression scale (CES-D) for Depressive symptoms and a single-item life satisfaction measure) and sleep quality (Pittsburgh Sleep Quality Index, PSQI) measures were conducted as part of the survey. Multiple imputation was used to deal with missing data in outcome, exposures or covariates. Relative excess risk for interaction (RERI) and its 95% confidence intervals (CIs) were estimated using adjusted prevalence odds ratios.

Results: We observed an association between depressed mood (5-units increase in CES-D score) (POR=1.7 [95%CI = 1.6 ; 1.8]) and sleep complaints and between low LS (not very satisfied vs. very satisfied) (POR=1.5 [1.1 ; 2.2]) and sleep complaints. Also, we observed a synergistic effect between lower level of LS (not very satisfied) and depressed mood (score ≥ 16) on prevalence of sleep disorders (RERI = 3.7 [-0.2 ; 7.1]). Furthermore, these findings were corroborated in sensitivity analysis done with the complete case dataset and in sex-specific analyses (RERI = 5.5 [-0.4 ; 11.3] and RERI = 2.4 [-2.5 ; 7.4] for men and women, respectively).

Conclusions: Both depressed mood and LS are notably associated with sleep quality and these relationships are best captured by considering their joint effects. Depression and LS need to be taken in consideration when analyzing sleep quality.

Strengths and limitations

- Strengths: this study draws its strength from its size and from the fact that it is a population-based sample, with well-defined health outcomes, and inclusion of an exhaustive list of relevant covariates.
- Limitations: our sample consisted of adults with a restricted age range (51 - 81 years) and as with any cross-sectional design, the directionality of the observed associations cannot be determined.

INTRODUCTION

Sleep is an important source of general health and well-being.[1] Sleep disturbances have been associated with health problems, including poor self-rated health, psychological conditions, chronic medical conditions, and mortality.[2] The prevalence of sleep disturbances in the population is dependent on its definition, and it ranges from 6% (clinical diagnosis of insomnia) to 48% (difficulties in initiating or maintaining sleep or early morning awakening).[3] Considering its high prevalence and association with health conditions, there is a need to investigate the factors associated with sleep disturbances in order to develop strategies to prevent or delay its onset.

Depressive symptomatology is an affective disorder in which the prevailing emotional mood of a person is negatively distorted or inappropriate to the circumstances and is sustained over a particular period of time.[4] Depressive symptoms are considered an important risk factor for insomnia and conversely, sleep disturbances are very common (60-80% prevalence) among depressed patients.[2] In patients with depressive symptoms, insomnia appears either previously (40%) or simultaneously (22%) with other psychological, physical and social symptoms.[5] Following the International Classification of Disease, tenth revision (ICD-X) definition, sleep disturbances are very clearly a symptom of depression, and do not precede it. But sleep complaints are a predictor for depressive relapse if they are a residual symptom after remission.[6] Though, a recent meta-analysis has shown that sleep disturbances can also lead to depression.[7] Also, in a recent systematic review of 9 cohort studies (8 longitudinal and 1 retrospective), the available evidence suggested that sleep disturbances and depression were bidirectionally associated.[8]

Life satisfaction (LS), is a component of subjective well-being.[6] It refers to cognitive judgments that remain quite constant even over a longer period of time.[9 10] A review revealed that subjective well-being, and not only the absence of mental illness, has an effect on all-cause morbidity and mortality.[11] In addition, LS is related to health predictors such as favorable self-reported health, social support, and positive health behaviors.[12] Several studies have shown moderate correlations between life satisfaction (LS) and depressive symptoms, and support independency indicating that research on indicators of well-being adds a distinctive dimension to psychiatric research.[13]

While there are numerous studies associating depression with poor sleep quality (for a review see [14]), there have been fewer studies evaluating associations of well-being and sleep quality. Cross-sectional studies have shown that lower well-being is associated with lower sleep quality.[15-17] Additionally these associations appear to be independent of psychological stressors.[18] It would therefore appear that not only depression is associated with sleep quality, but also well-being, on its own, is associated with sleep quality in the general population. Previous research has shown that depressive symptoms, a transitional period of low mood (state), are associated with worse sleep quality.[19] However, it has not yet been investigated whether well-being, which tends to be stable over time (trait), can alter that association. Recent research has shown that the relationship of mood and sleep quality is best captured by considering the joint effects of both stable and unstable aspects of mood.[17] Steptoe et al. reported that the benefits of sleep are enhanced by high well-being and this independently of depressed mood.[20] Formerly Diener et al. reported that people who experienced intense well-being were more likely to experience intense depressed mood as well.[21] It has also been reported that highly cheerful people are more likely to engage in risky

health behaviors.[22] Therefore there is some support for the hypothesis that different levels of LS might modify the association between depressive symptomatology and sleep quality.

Aims

This study focuses on the association between depressive symptoms and sleep disturbances and whether this association can be modified by LS. The current study aims to extend our understanding of the relationship between depressive symptoms and the presence of sleep disturbances. In particular, using cross-sectional data from the Heinz Nixdorf Recall Study (2006-2008), we assessed the presence of an interaction between depression and LS on sleep quality, by studying whether the joint effect of exposure to both factors was greater than the sum of their independent effects. We hypothesized that: a) depressive symptoms would negatively relate to sleep quality; b) LS would be positively associated with sleep quality and c) LS would modulate the relation between depressive symptoms and sleep quality. While an explanation of this link cannot be advanced in the frame of a cross-sectional study it seems nevertheless justified to examine the hypothesis that LS modifies this association, such that stronger associations of depressive symptoms with sleep quality are observed among adults with lower LS.

MATERIALS AND METHODS

Study population and study sample

Data were derived from the Heinz Nixdorf Recall (Risk Factors, Evaluation of Coronary Calcium and Lifestyle) Study: a cross-sectional analysis of participants in the follow-up survey when sleep quality and mood assessments took place. The design of the study has been previously described in detail.[23] Briefly, during the baseline examination between December 2000 and August 2003, a total of 4,814 subjects aged between 45 and 75 years were recruited from three adjacent cities in the German Ruhr Area: Essen, Bochum, Mülheim/Ruhr.[23 24] The baseline recruitment proportion was 56%.[25] All subjects were invited for re-examination in 2006-2008. Overall, 154 out of 4,814 subjects (3%) died before re-examination, 503 refused examination (10%) leading to a final 5-years follow-up group of 4,157 subjects (87%). Data collection at follow-up was done through standardized interviews, clinical examination, comprehensive laboratory tests and self-administered questionnaires. The Heinz Nixdorf Recall study was approved by the institutional local ethics committee and has therefore been performed in accordance with the ethical standards laid out in the 1964 Declaration of Helsinki and its later amendments. An internal and external quality management system was established according to industrial standard norms DIN ISO 9001:2000/2008. All participants gave written informed consent.

Outcome

Sleep quality and sleep disturbances in the past month were measured through the Pittsburgh sleep quality index (PSQI).[26] The 19 self-rated items are combined to form seven

component scores, each of which has a range of 0-3 points. A score of "0" indicates no difficulty, while a score of "3" indicates severe difficulties. The seven component scores are then added to yield one "global" score, with a range of 0-21 points, "0" indicating no difficulty and "21" indicating severe sleep disturbances. For the purposes of our study, we examined the PSQI global score, which was calculated using the algorithm outlined in Buysse et al.[26] A PSQI global score greater than 5 was classified as poor quality sleep.[20]

Major exposures

Depressive symptoms last week was assessed by self-administered questionnaire through the 15 items Center for Epidemiologic Studies Depression scale (CES-D 15).[27 28] We modified the CES-D scale by excluding the symptom "my sleep was restless" to remove the item's correlation with questions on sleep disturbances.[29] Thus, the scale had 14 items and a score range 0 to 42, with higher scores indicative of more symptomatology. A cut-off of 18 has been suggested for depressive symptoms screening in the German population.[30] Because of the removal of an item we considered various cutoffs for depressive symptoms (16 and 18).

LS was measured by self-administered questionnaire through the following question: "how satisfied are you with your personal life?" Answer categories were: very satisfied; usually satisfied; unsatisfied.[31 32] The item-total correlation of this question with the items of the Satisfaction With Life Scale (SWLS) has been reported to be 0.75.[33] Additionally, recent studies have shown that similar single-item LS measures showed a good criterion validity with the SWLS (r=0.62).[34] For analysis purposes we dichotomized this item in "very satisfied"

vs. “not very satisfied”, because only 6% of the population was categorized as “unsatisfied”. There were no differences in sex distribution, alcohol consumption, BMI, cholesterol level, hypertension status or education level among participants in each life satisfaction category. But those participants that were unsatisfied were younger, suffered more often from depressed mood, sleep disturbances, life events, had lower SNI, were more often current smokers and physically inactive. In our sample, we tested the association between the dichotomous LS and the CES-D score with logistic regression analysis and was only moderate (OR=0.9, CI=0.8 ; 0.9 in a crude model and OR= 0.8, CI=0.8 – 0.8 in an age and sex-adjusted model).

Covariates

Covariates known to affect sleep quality (outcome), that were also associated with either depressive symptoms or LS (exposures of interest) were identified from the literature[14-18] and discussed prior to the analyses. Socio-demographic variables: age, sex and socioeconomic status were obtained at baseline. Education was used as a proxy for the socio-economic status, classified in years of formal education according to the “International Standard Classification of Education” combining school and vocational training. Four categories were defined with the highest category of 18 and more years of education (equivalent to a University degree), category 3 with 14 to 17 years, category 2 with 11 to 13 years and the lowest category of 10 and less years (equivalent to a basic school degree and no vocational training). Anthropometric measurements (weight and height, body mass index (BMI)=kg/m^2) and blood pressure were determined at the clinical examination. Lifestyle factors were determined through personal interview (alcohol consumption and smoking

habits). Social support, physical activity and life events were determined in the standardized interview. Social support was characterized with the Berkman-Syme's Social Network Index.[35] The components of the index are weighted in an algorithm resulting in four categories (I: low, II: mid-low, III: mid-high, IV: high). Physical activity was assessed by asking participants about the kind and duration of exercise performed in the preceding month, whereby 'physically inactive' meant having performed no exercise at all.[36] In the self-administered questionnaire participants were asked to report whether any stressful life events had occurred in the past 6 months, to which they could answer yes or no. Self-rated health was assessed in the interview by one question ('How would you, referring to the last twelve months, describe your overall health status?') on a 5-point Likert-scale ('very good', 'good', 'moderate', 'poor' and 'very poor').

Statistical Methods

The present study includes only the 3,880 participants at follow-up (89% of the follow-up participants) who filled in the questionnaire. We identified minimally sufficient adjustment sets using diagrams that represent the relations among the exposure, outcome, and other variables.[37] All previously mentioned covariates were considered potential adjustment variables for the relation of LS and depressive symptoms with sleep quality. The minimally sufficient adjustment set for the association of LS and sleep quality included age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, modified CES-D, social support, life events, and physical activity. The minimally sufficient adjustment set for the association of depressive symptoms and sleep quality included age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, LS, social support, life events, and physical activity.

We used multivariable logistic regression to estimate PORs (prevalence odds ratio) that account for depressive symptoms and LS on sleep quality. Exposures were analyzed dichotomously (CES-D score ≥16 vs. < 16 and LS=very satisfied vs. not very satisfied) and continuously (depressive symptoms per 5 unit increase, previously reported as clinically relevant) or categorically (LS 3 categories).[38] Seven hundred twenty two of 3,880 (19%) subjects had missing data for sleep quality, depressive symptoms, LS or covariates. To manage missing data we undertook multiple imputation, using the MI procedure in SAS. We generated an imputed database containing 20 imputed versions using all relevant variables predicting missingness (PSQI score, life satisfaction, CES-D score, age, alcohol consumption, BMI, blood pressure, cholesterol level, life events, sport index score, sex, smoking status, SNI and education level). Regression results were combined using the MIANALYZE procedure in SAS. We explored the pattern of missing data and performed sensitivity analyses on complete cases. Furthermore, we studied the presence of interaction (relative excess risk due to interaction [RERI]) between depressive symptoms and LS by comparing the joint effects of exposure to both factors with the sum of their independent effects. The estimated RERI was calculated as follows:[39]

$$RERI = OR_{11} - OR_{10} - OR_{01} + 1$$

where OR_{11} denotes OR among those exposed to both factors (depressive symptoms and low LS). A RERI of 0 means no interaction, a RERI > 1 means interaction without

monotonicity assumption for one exposure and a RERI > 2 means interaction even without monotonicity assumption for both exposures.[39 40] We performed several sensitivity analyses with the complete case dataset (N=3158). In the first sensitivity analysis, we assumed that both depressive symptoms and sleep quality are strongly sex-dependent, therefore we did sex-stratified interaction analysis to investigate sex-specific patterns. In the second analysis, a higher cut-off for the depression scale (CES-D) was chosen, in order to investigate the robustness of our results. In a third analysis, exposures were treated as continuous (depressive symptoms) or categorical (LS) variables. We have calculated and reported confidence intervals to assess the precision of our estimates because our goal is the estimation and not significance testing. We wish to avoid publication bias by preferential reporting of significant results. Instead, we judge the value of our estimates by their precision and validity. All analyses were performed using SAS 9.3. (SAS Inc., Cary, NC).

RESULTS

Sample characteristics

A total of 1,932 participants (50%) were classified in the "good sleep quality" group which consisted of 57% men with a mean age of 64.4 years (SD 7.5, 51 to 81 years). A total of 1,477 participants (38%) were classified in the “sleep disturbances” category which was 38% male with a mean age of 65.3 years (SD 7.6). A further 471 participants (12%) did not answer the PSQI questionnaire. Table 1 shows demographic and clinical characteristics of participants stratified by sleep quality. Most clinical risk factors (age, hypertension, BMI, cholesterol and physical activity) were not different between the index population of “good sleep quality” and the “sleep disturbed” subgroup. On the contrary, most socio-demographic and psychological variables, e.g. educational level, self-rated health, social network index, life events, depressive symptoms and LS, showed different prevalences between subgroups. Additionally, participants in the good sleep quality group were more often men, current or former smokers and consumed more alcohol.

Association of depressive symptoms and life satisfaction with sleep quality

Table 2 presents the POR estimates for sleep quality with depressive symptoms as a continuous variable (data are shown per 5 unit increments in CES-D scale) and LS as a categorical variable. Similar results were obtained with complete case analysis and multiple imputation, thus we report effect estimates from the multiple imputation analyses. For “depressive symptoms” there was a strong association between depressive symptoms (higher scores in CES-D; 5-units increment) and sleep disturbances (POR = 1.7, 95%CI 1.6 ; 1.8). The results of the logistic regression indicate that participants reporting lower LS

(unsatisfied) had an increased prevalence of suffering from sleep disturbances compared with participants reporting higher LS (very satisfied) (POR =1.5, 95%CI 1.1 ; 2.2). The results of the logistic regression with depression and LS dichotomized are presented in supplementary table 1. The results indicate that participants with higher CES-D scores (depressive symptoms; scores ≥ 16) had an increased prevalence of suffering from sleep disturbances than non-depressed participants (POR = 4.8, 95%CI 3.6 ; 4.5). Participants reporting lower LS had an increased prevalence of suffering from sleep disturbances compared with participants reporting higher LS (POR =1.6, 95%CI 1.3 ; 1.8).

Interaction between LS and depressive symptoms on the prevalence of sleep disturbances

The combined effects of depressive symptoms and LS on sleep quality were greater than the sums of the separate estimated effects (table 3 and supplementary table 2). Multiple imputation and complete case analysis yielded very similar results, thus we report here results from multiple imputation. The RERI for depressive symptoms (score ≥ 16 in the CES-D scale) and LS was 3.7 (95%CI=-0.2 ; 7.1), which indicates that because of the interaction between depressive symptoms and LS, the POR is 3.7 times higher than expected from the addition of the separate effects of depressive symptoms and LS alone. Results for complete case analysis were comparable and are presented in supplementary table 2.

Sensitivity analysis

Several sensitivity analyses in the complete case dataset were performed. Sex-stratified interaction analysis produced similar results (RERI = 2.4 [-2.5 ; 7.4] and RERI= 5.5 [-0.4 ; 11.3]

for women and men respectively) (supplementary tables 3 and 4), but have to be interpreted with caution due to the small numbers of participants in some of the categories. The additive interaction obtained with a higher cut-off for the CES-D scale (scores ≥ 18) was RERI = 4.2 (95%CI=-1.9 ; 10.4). We repeated the interaction analysis with depressive symptoms considered continuously (CES-D score 0 to 42, per 5-unit increase) and LS in 3-categories. The results of this logistic regression indicate that participants with higher CES-D scores (score 15-20) had an increased prevalence of suffering from sleep disturbances than participants with lower scores (score 0-5) (POR = 1.9; 95%CI=1.6 ; 2.3). Participants more dissatisfied with life ("not very satisfied") had an increased prevalence of suffering from sleep disturbances compared with participants satisfied with life ("very satisfied") (POR = 1.5; 95%CI=0.6 ; 3.9). Moreover, the RERI for depressive symptoms and LS (assessed by comparing "very satisfied" with "not very satisfied" and a CES-D score of 0 to a score of 16) was 5.4 (95%CI=-10.0 ; 20.8) (data not shown).

DISCUSSION

Findings from the current study showed that both depressive symptoms and LS were notably associated with sleep quality, emphasizing the importance of both stable and dynamic features of mood on sleep patterns. In agreement with previous studies, we found a negative relation between sleep and depressive symptoms [14] and an overall positive relation between good sleep quality and LS.[15-18] Furthermore, our results suggested that these relationships were best captured by considering the joint effects of depressive symptoms and LS, with higher depressive symptoms associated with substantially worse sleep quality, especially among individuals with lower LS.

Depressive symptoms and LS were only moderately inversely related in our population. This confirms previous literature reporting that they are distinct constructs.[13 41] Sleep disturbances are part of the diagnostic criteria for depression in ICD-10 and DSM-IV; therefore it is not surprising that CES-D and PSQI scores are so strongly associated. A number of previous studies have shown that depressive symptoms are related to poorer sleep in the adult population with OR of 1.5 to 3.0 in most studies.[2 42] Our results showed a higher POR for depressive symptoms (4.8, 95%CI 3.6 ; 6.5), probably due to the relatively high cut-off chosen in this study. Additionally, the OR for LS was similar to those previously reported, between 1.8 and 2.1 (POR=1.6, 95%CI=1.3 ; 1.8).[43 44] Although in concordance with those findings, the present results extend them in several important ways. Most notably, our study examined interaction effects of LS and depressive symptoms on sleep quality.

Ong et al. examined a similar interaction, however only on the multiplicative scale in which they showed that well-being interacts with negative reactivity on overall sleep quality.[17] These results were expanded on the additive scale in our study. The additive interaction analysis examined whether the relative detriment of depressive symptoms on sleep quality was the same across LS groups. We found that participants with depressive symptoms had much worse sleep quality if they belonged to the non-satisfied group than if they belonged to the satisfied group (multiplicative interaction POR = 1.5, 95%CI= 0.6 ; 3.6). However, from a public health perspective, additive interaction is the relevant one, as it can help determine which subgroups would benefit most from a given treatment, i.e. psychotherapy to improve depressive symptoms and thus sleep quality in those participants with low LS. The additive interaction (RERI=3.7, 95%CI=-0.2 ; 7.1) indicates that there is a synergistic effect between depressive symptoms and LS, which substantially increased the prevalence of worse sleep quality. Our study suggests that the depressive symptoms-sleep quality association was modified by LS level in additive interaction analyses.

This study draws its strength from its size and from the fact that it is a population-based sample with well-defined health outcomes and inclusion of an exhaustive list of relevant covariates. Nevertheless, our conclusions are limited by several factors. Our sample consisted of adults with a restricted age range (51 - 81 years) and as with any cross-sectional design, the directionality of the observed associations cannot be determined. Given the age range of the study participants, it is possible that our results cannot be generalised to the complete age range of adults. Women in the post-menopausal period suffer more often than younger and older women from sleep disturbances, depressive symptoms and/or pain. Also men in this age range can present more often pain symptoms. Regarding the

representability of this study population, it has been previously reported that high social class and good health status were overrepresented at baseline of the Heinz Nixdorf Recall Study.[25] Moreover, we used a modified version of the CES-D scale to measure depressive symptoms. Because of this modification, we could not consider previously validated cut-offs for our population. Therefore, we ran sensitivity analyses with various cut-offs (16 and 18) in order to identify relevant changes. In the present study, we did not use sex-specific cut-offs to detect depressive symptoms as previously described in the literature.[45] However, it has been recently reported that several depression tests (Beck Depression Inventory - II, Inventory of Depressive Symptoms - self-report and the Montgomery-Asberg Depression Rating Scale) should use different cut-offs for men and women to better discriminate between depressed and non-depressed participants. Yet, they also affirm that it is too early to recommend gender specific reference values for those tests and that previous studies have found no sex differences for depression scales.[46] Our assessment of LS with a single-item question was limited; however, a recent study has shown that single-item life satisfaction measures performed very similarly compared to the multiple-item SWLS, a more psychometrically established measure.[34] Also, outcome and predictors (sleep quality, depressive symptoms and LS) have been analyzed as dichotomous variables, though they were documented as continuous. Nevertheless, we ran sensitivity analyses with continuous (depressive symptoms) and categorical (LS) exposure variables in complete case analysis in order to identify relevant changes. Finally, the RECALL study was not powered for this research question; therefore some estimates are very imprecise.

These results extend the study of depressive symptoms, LS and sleep quality and suggest that the association between depressive symptoms and sleep quality is modified by LS.

Understanding the predictors of poor sleep quality may have important implications for future health outcomes, such as development of chronic medical conditions.

Contributor statement: ASP, ND, SM, SD, SM, AS, HK, RE and AS contributed to the study design and data acquisition. AS supervised all aspects of the study's execution. MEL planned the analysis and undertook the primary analysis and wrote the first draft of the paper. All authors critically reviewed the paper and approved the submitted version.

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Table 1. Demographic and clinical characteristics of participants stratified by sleep quality.

Data are presented as n (%) unless otherwise stated.

			Sleep quality	
Variable		**Total**	**Good [a]** **(N = 1932)**	**Poor [b]** **(N = 1477)**
Sex	Women: n (%, CI)	1746	823 (42.6: 40.4 – 44.8)	923 (62.5: 60.0 – 65.0)
	Men: n (%, CI)	1663	1109 (57.4: 55.2 – 59.6)	554 (37.5: 35.0 – 40.0)
Education	< 10 years: n (%, CI)	324	140 (7.3: 6.1 – 8.4)	184 (12.5: 10.8 – 14.1)
	11 – 13 years: n (%, CI)	1910	1005 (52.0: 49.8 – 54.2)	905 (61.3: 58.8 – 63.8)
	14 – 17 years: n (%, CI)	791	531 (27.5: 25.5 – 29.5)	260 (17.6: 15.7 – 19.5)
	≥ 18 years: n (%, CI)	384	256 (13.3: 11.7 – 14.8)	128 (8.7: 7.2 – 10.1)
Smoking	Never smoker: n (%, CI)	1392	731 (39.0: 36.7 – 41.2)	661 (46.7: 44.1 – 49.3)
	Former smoker: n (%, CI)	1343	809 (43.1: 40.9 – 45.3)	534 (37.7: 35.2 – 40.2)
	Current smoker: n (%, CI)	558	337 (18.0: 16.2 – 19.7)	221 (15.6: 13.7 – 17.5)
Self-rated health	Very good: n (%, CI)	164	137 (7.3: 6.1 – 8.5)	27 (1.9: 1.2 – 2.6)
	Good: n (%, CI)	1314	922 (49.2: 46.9 – 51.4)	392 (27.7: 25.4 – 30.0)
	Fair: n (%, CI)	1275	645 (34.4: 32.2 – 36.5)	630 (44.5: 41.9 – 47.1)
	Poor: n (%, CI)	446	137 (7.3: 6.1 – 8.5)	309 (21.8: 19.7 – 24.0)
	Very poor: n (%, CI)	93	35 (1.9: 1.3 – 2.5)	58 (4.1: 3.1 – 5.1)
Social network index	I (low): n (%, CI)	856	443 (23.7: 21.8 – 25.6)	413 (29.2: 26.8 – 31.6)
	II: n (%, CI)	1254	715 (38.2: 36.0 – 40.4)	539 (38.1: 35.6 – 40.7)
	III: n (%, CI)	942	567 (30.3: 28.2 – 32.4)	375 (26.5: 24.2 – 28.8)
	IV (high): n (%, CI)	232	145 (7.8: 6.5 – 9.0)	87 (6.2: 4.9 – 7.4)
Hypertension [c]	Yes: n (%, CI)	1250	755 (40.4: 38.2 – 42.6)	495 (35.1: 32.6 – 37.6)
Physical activity	Active: n (%, CI)	1504	816 (43.5: 41.2 – 45.7)	688 (48.6: 46.0 – 51.2)
Life events in last 6 months	Yes: n (%, CI)	695	346 (18.2: 16.5 – 20.0)	349 (24.1: 21.9 – 26.3)
Depressed mood (CES-D ≥ 16) [d]	Yes: n (%, CI)	294	58 (3.1: 2.3 – 3.8)	236 (16.3: 14.4 – 18.3)

			Sleep quality	
Variable		**Total**	**Good [a]** **(N = 1932)**	**Poor [b]** **(N = 1477)**
Life satisfaction	Very satisfied: n (%, CI)	1194	778 (41.2: 39.0 – 43.4)	416 (28.9: 26.5 – 31.2)
	Quite satisfied: n (%, CI)	1943	1045 (55.4: 53.1 – 57.6)	898 (62.3: 59.8 – 64.8)
	Unsatisfied: n (%, CI)	192	65 (3.4: 2.6 – 4.3)	127 (8.8: 7.3 – 10.3)
Depressed mood: mean (SD) [d]		3338	5.3 (4.4)	9.5 (6.7)
Age years: mean (SD)		3409	64.4 (7.5)	65.3 (7.6)
BMI (kg /m^2) : mean (SD)		3287	28.1 (4.6)	28.3 (5.1)
Total Cholesterol mg/ dL: median (Q1;Q3)		3274	226 (199; 254)	223 (199; 249)
HDL Cholesterol mg/dL: median (Q1;Q3)		3274	59 (49; 71)	57 (48; 69)
Alcohol consumption ml/week: mean (SD)		3306	70.2 (102.7)	57.8 (107.6)

PSQI=Pittsburgh sleep quality index, CES-D= center for epidemiological studies depression scale, BMI=body mass index, HDL=high density lipoprotein. [a] Good sleep quality: PSQI score ≤ 5. [b] Poor sleep quality: PSQI score > 5. [c] Participants on antihypertensive medication or with systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg were defined as hypertensive. [d] CES-D scale excludes the item “my sleep was restless

Table 2. Association of depressed mood and life satisfaction with sleep quality. PORs per 5 unit increment in CES-D scale (depressed mood).

		Complete case analysis		Multiple imputation	
Model	**Adjusted for:**	**N**	**POR (95%CI)**	**N**	**POR (95%CI)**
Depressed mood (score 0 – 42; unit increment=5)					
1	-	3338	2.0 (1.8 – 2.1)	3880	1.8 (1.7 – 1.9)
2	Age and sex	3338	1.9 (1.8 – 2.1)	3880	1.8 (1.6 – 1.9)
3	Fully adjusted [a]	3163	1.8 (1.7 – 2.0)	3880	1.7 (1.6 – 1.8)
Life satisfaction (very -, quite satisfied, unsatisfied)					
1	-	3329		3880	
	Very vs. unsatisfied		3.7 (2.6 – 5.0)		3.6 (2.6 – 4.9)
	Quite vs. unsatisfied		2.3 (1.7 – 3.1)		2.3 (1.7 – 3.1)
2	Age and sex	3329		3880	
	Very vs. unsatisfied		4.2 (3.0 – 5.8)		4.2 (3.0 – 5.7)
	Quite vs. unsatisfied		2.4 (1.7 – 3.2)		2.4 (1.7 – 3.3)
3	Fully adjusted [b]	3163		3880	
	Very vs. unsatisfied		1.5 (1.0 – 2.2)		1.5 (1.1 – 2.2)
	Quite vs. unsatisfied		1.2 (0.9 – 1.8)		1.3 (0.9 – 1.8)

POR=prevalence odds ratio, CI=confidence interval.

[a] Fully adjusted: age, sex, alcohol consumption, BMI (body mass index), blood pressure, total cholesterol, life satisfaction, life events, physical activity, education years, smoking and social support

[b] Fully adjusted: age, sex, alcohol consumption, BMI (body mass index), blood pressure, total cholesterol, CES-D score (center for epidemiological studies depression scale), life events, physical activity, education years, smoking and social support

Table 3. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems (multiple imputation, N=3880)

	Life satisfaction	
	very satisfied	not very satisfied
	POR (95% CI)	POR (95% CI)
Non-depressed mood (cut-off < 16)	1.0	1.5 (1.3 ; 1.8)
Depressed mood (cut-off ≥ 16)	3.4 (1.5 ; 7.9)	7.4 (3.5 ; 11.3)

POR=prevalence odds ratio, CI=confidence interval.

Measure of interaction on additive scale: RERI (95% CI) = 3.7 (-0.2 ; 7.1)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

Supplementary table 1. Association of depressed mood and life satisfaction with sleep quality.

		Complete case analysis		Multiple imputation	
Model	**Adjusted for:**	**N**	**POR (95%CI)**	**N**	**POR (95%CI)**
Depressed mood (<16 not depressed vs. ≥ 16 depressed mood (ref.))					
1	-	3338	6.2 (4.6 – 8.3)	3880	6.4 (4.8 – 8.5)
2	Age and sex	3338	5.8 (4.3 – 7.9)	3880	6.0 (4.5 – 8.0)
3	Age, sex, alcohol consumption, BMI, blood pressure, total cholesterol, life satisfaction, life events, physical activity, education years, smoking and social support	3158	4.6 (3.3 – 6.3)	3880	4.8 (3.6 – 4.5)
Life satisfaction (very satisfied vs. not very satisfied (ref.))					
1	-	3329	1.7 (1.5 – 2.0)	3880	1.7 (1.5 – 1.9)
2	Age and sex	3329	1.9 (1.6 – 2.2)	3880	1.9 (1.6 – 2.2)
3	Age, sex, alcohol consumption, BMI, blood pressure, total cholesterol, CES-D score, life events, physical activity, education years, smoking and social support	3158	1.6 (1.4 – 1.9)	3880	1.6 (1.3 – 1.8)

CES-D= center for epidemiological studies depression scale, BMI=body mass index, POR=prevalence odds ratio, CI=confidence interval.

Supplementary table 2. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems (N=3158)

	Life satisfaction				
	very satisfied		not very satisfied		**POR (95% CI) for life satisfaction within strata of depressed mood**
	N good sleep quality/ N poor sleep quality	POR (95% CI)	N good sleep quality/ N poor sleep quality	POR (95% CI)	
Non-depressed mood (cut-off < 16)	380 / 733	1.0	769 / 1011	1.6 (1.3 ; 1.8)	1.6 (1.3 ; 1.8)
Depressed mood (cut-off ≥ 16)	16 / 7	3.2 (1.3 ; 8.0)	195 / 47	7.3 (5.1 ; 10.4)	2.1 (0.8 ; 5.9)
POR (95% CI) for depressed mood within strata of LS		3.2 (1.3 ; 8.0)		4.2 (3.3 ; 6.6)	

Measure of interaction on additive scale: RERI (95% CI) = 3.6 (-0.2 ; 7.4)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

Supplementary table 3. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems for women (N=1604)

	Life satisfaction				
	very satisfied		not very satisfied		**POR (95% CI) for life satisfaction within strata of depressed mood**
	N sleep problems / no sleep problems	POR (95% CI)	N sleep problems / no sleep problems	POR (95% CI)	
Non-depressed mood (cut-off < 16)	248 / 337	1.0	450 / 396	1.6 (1.3 ; 2.0)	1.6 (1.3 ; 2.0)
Depressed mood (cut-off ≥ 16)	13 / 4	3.6 (1.1 ; 11.3)	130 / 26	6.6 (4.1 ; 10.5)	1.8 (0.4 ; 7.5)
POR (95% CI) for depressed mood within strata of LS		3.6 (1.1 ; 11.3)		4.2 (2.7 ; 6.7)	

Measure of interaction on additive scale: RERI (95% CI) = 2.4 (-2.5 ; 7.4)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

Supplementary table 4. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems for men (N=1554)

	Life satisfaction				**POR (95% CI) for life satisfaction within strata of depressed mood**
	very satisfied		not very satisfied		
	N sleep problems / no sleep problems	POR (95% CI)	N sleep problems / no sleep problems	POR (95% CI)	
Non-depressed mood (cut-off < 16)	132 / 396	1.0	319 / 615	1.5 (1.2 ; 2.0)	1.5 (1.2 ; 2.0)
Depressed mood (cut-off ≥ 16)	3 / 3	2.4 (0.5 ; 12.4)	65 / 21	8.4 (4.9 ; 14.5)	5.5 (0.6 ; 47.5)
POR (95% CI) for depressed mood within strata of LS		2.4 (0.5 ; 12.4)		5.4 (3.2 ; 9.1)	

Measure of interaction on additive scale: RERI (95% CI) = 5.5 (-0.4 ; 11.3)

Measure of interaction on multiplicative scale: ratio of PORs (95% CI) = 2.3 (0.4 ; 12.6)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Depressive symptoms, life satisfaction, and prevalence of sleep disturbances in the general population of Germany. Results from the Heinz Nixdorf Recall Study.

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Word count: 46 references, 3726 main text, 3 tables, 4 supplementary tables

Abstract

Objectives: It appears that not only depression, but also low life satisfaction (LS) is related to sleep complaints in the general population. We evaluate whether the prevalence of sleep complaints attributable to depressed mood is greater among participants with low LS.

Setting, participants and outcome measures: Analysis of cross-sectional data from 3,880 cohort members from the German Heinz Nixdorf Recall study (2006-2008) aged 51 to 81 years. Standard mood (Center for Epidemiological Studies Depression scale (CES-D) for Depressive symptoms and a single-item life satisfaction measure) and sleep quality (Pittsburgh Sleep Quality Index, PSQI) measures were conducted as part of the survey. Multiple imputation was used to deal with missing data in outcome, exposures or covariates. Relative excess risk for interaction (RERI) and its 95% confidence intervals (CIs) were estimated using adjusted prevalence odds ratios. Due to the study size, is the precision of the measures of additive interaction relatively low.

Results: We observed an association between depressed mood (5-units increase in CES-D score) (POR=1.7 [95%CI = 1.6 ; 1.8]) and sleep complaints and between low LS (not very satisfied vs. very satisfied) (POR=1.5 [1.1 ; 2.2]) and sleep complaints. Also, we observed a synergistic effect between lower level of LS (not very satisfied) and depressed mood (score ≥ 16) on prevalence of sleep disorders (RERI = 3.7 [-0.2 ; 7.1]). Furthermore, these findings were corroborated in sensitivity analysis done with the complete case dataset and in sex-specific analyses (RERI = 5.5 [-0.4 ; 11.3] and RERI = 2.4 [-2.5 ; 7.4] for men and women, respectively).

Conclusions: Both depressed mood and LS are notably associated with sleep quality and these relationships are best captured by considering their joint effects. Depression and LS need to be taken in consideration when analyzing sleep quality.

Strengths and limitations

- Strengths: this study draws its strength from its size and from the fact that it is a population-based sample, with well-defined health outcomes, and inclusion of an exhaustive list of relevant covariates.
- Limitations: our sample consisted of adults with a restricted age range (51 - 81 years) and as with any cross-sectional design, the directionality of the observed associations cannot be determined. The precision of our measures of additive interaction (RERI) was quite low because of the sample size.

INTRODUCTION

Sleep is an important source of general health and well-being.[1] Sleep disturbances have been associated with health problems, including poor self-rated health, psychological conditions, chronic medical conditions, and mortality.[2] The prevalence of sleep disturbances in the population is dependent on its definition, and it ranges from 6% (clinical diagnosis of insomnia) to 48% (difficulties in initiating or maintaining sleep or early morning awakening).[3] Considering its high prevalence and association with health conditions, there is a need to investigate the factors associated with sleep disturbances in order to develop strategies to prevent or delay its onset.

Depressive symptomatology is an affective disorder in which the prevailing emotional mood of a person is negatively distorted or inappropriate to the circumstances and is sustained over a particular period of time.[4] Depressive symptoms are considered an important risk factor for insomnia and conversely, sleep disturbances are very common (60-80% prevalence) among depressed patients.[2] In patients with depressive symptoms, insomnia appears either previously (40%) or simultaneously (22%) with other psychological, physical and social symptoms.[5] Following the International Classification of Disease, tenth revision (ICD-X) definition, sleep disturbances are very clearly a symptom of depression, and do not precede it. But sleep complaints are a predictor for depressive relapse if they are a residual symptom after remission.[6] Though, a recent meta-analysis has shown that sleep disturbances can also lead to depression.[7] Also, in a recent systematic review of 9 cohort studies (8 longitudinal and 1 retrospective), the available evidence suggested that sleep disturbances and depression were bidirectionally associated.[8]

Life satisfaction (LS), is a component of subjective well-being.[6] It refers to cognitive judgments that remain quite constant even over a longer period of time.[9 10] A review revealed that subjective well-being, and not only the absence of mental illness, has an effect on all-cause morbidity and mortality.[11] In addition, LS is related to health predictors such as favorable self-reported health, social support, and positive health behaviors.[12] Several studies have shown moderate correlations between life satisfaction (LS) and depressive symptoms, and support independency indicating that research on indicators of well-being adds a distinctive dimension to psychiatric research.[13]

While there are numerous studies associating depression with poor sleep quality (for a review see [14]), there have been fewer studies evaluating associations of well-being and sleep quality. Cross-sectional studies have shown that lower well-being is associated with lower sleep quality.[15-17] Additionally these associations appear to be independent of psychological stressors.[18] It would therefore appear that not only depression is associated with sleep quality, but also well-being, on its own, is associated with sleep quality in the general population. Previous research has shown that depressive symptoms, a transitional period of low mood (state), are associated with worse sleep quality.[19] However, it has not yet been investigated whether well-being, which tends to be stable over time (trait), can alter that association. Recent research has shown that the relationship of mood and sleep quality is best captured by considering the joint effects of both stable and unstable aspects of mood.[17]

There is some support for the assumption that different levels of LS might differentially affect the association between depressive symptomatology and sleep quality. Several studies have shown that resilience, the ability to prosper despite stress and adversity is

associated with LS,[20 21] or that even it can foster LS.[22 23] Moreover, resilience has been associated with better health outcomes in the face of stress and adversity.[24 25] Therefore, it can be assumed that, for participants with higher LS (thus more resilient) the depressive symptomatology would have weaker effects on their sleep quality; whereas for participants with lower LS (and thus less resilient), small levels of depressive symptomatology could lead to greater sleep disturbances.

Aims

This study focuses on the association between depressive symptoms and sleep disturbances and whether this association can be modified by LS. The current study aims to extend our understanding of the relationship between depressive symptoms and the presence of sleep disturbances. In particular, using cross-sectional data from the Heinz Nixdorf Recall Study (2006-2008), we assessed the presence of an interaction between depression and LS on sleep quality, by studying whether the joint effect of exposure to both factors was greater than the sum of their independent effects. We hypothesized that: a) depressive symptoms would negatively relate to sleep quality; b) LS would be positively associated with sleep quality and c) LS would modulate the relation between depressive symptoms and sleep quality. While an explanation of this link cannot be advanced in the frame of a cross-sectional study it seems nevertheless justified to examine the hypothesis that LS modifies this association, such that stronger associations of depressive symptoms with sleep quality are observed among adults with lower LS.

MATERIALS AND METHODS

Study population and study sample

Data were derived from the Heinz Nixdorf Recall (Risk Factors, Evaluation of Coronary Calcium and Lifestyle) Study: a cross-sectional analysis of participants in the follow-up survey when sleep quality and mood assessments took place. The design of the study has been previously described in detail.[26] Briefly, during the baseline examination between December 2000 and August 2003, a total of 4,814 subjects aged between 45 and 75 years were recruited from three adjacent cities in the German Ruhr Area: Essen, Bochum, Mülheim/Ruhr.[26 27] The baseline recruitment proportion was 56%.[28] All subjects were invited for re-examination in 2006-2008. Overall, 154 out of 4,814 subjects (3%) died before re-examination, 503 refused examination (10%) leading to a final 5-years follow-up group of 4,157 subjects (87%). Data collection at follow-up was done through standardized interviews, clinical examination, comprehensive laboratory tests and self-administered questionnaires. The Heinz Nixdorf Recall study was approved by the institutional local ethics committee and has therefore been performed in accordance with the ethical standards laid out in the 1964 Declaration of Helsinki and its later amendments. An internal and external quality management system was established according to industrial standard norms DIN ISO 9001:2000/2008. All participants gave written informed consent.

Outcome

Sleep quality and sleep disturbances in the past month were measured through the Pittsburgh sleep quality index (PSQI).[29] The 19 self-rated items are combined to form seven

component scores, each of which has a range of 0-3 points. A score of "0" indicates no difficulty, while a score of "3" indicates severe difficulties. The seven component scores are then added to yield one "global" score, with a range of 0-21 points, "0" indicating no difficulty and "21" indicating severe sleep disturbances. For the purposes of our study, we examined the PSQI global score, which was calculated using the algorithm outlined in Buysse et al., where a PSQI global score greater than 5 was classified as poor quality sleep.[29]

Major exposures

Depressive symptoms last week was assessed by self-administered questionnaire through the 15 items Center for Epidemiologic Studies Depression scale (CES-D 15).[30 31] We modified the CES-D scale by excluding the symptom "my sleep was restless" to remove the item's correlation with questions on sleep disturbances.[32] Thus, the scale had 14 items and a score range 0 to 42, with higher scores indicative of more symptomatology. A cut-off of 18 has been suggested for depressive symptoms screening in the German population.[33] Because of the removal of an item we considered various cutoffs for depressive symptoms (16 and 18).

LS was measured by self-administered questionnaire through the following question: "how satisfied are you with your personal life?" Answer categories were: very satisfied; usually satisfied; unsatisfied.[34 35] The item-total correlation of this question with the items of the Satisfaction With Life Scale (SWLS) has been reported to be 0.75.[36] Additionally, recent studies have shown that similar single-item LS measures showed a good criterion validity with the SWLS (r=0.62).[37] For analysis purposes we dichotomized this item in "very satisfied"

vs. “not very satisfied”, because only 6% of the population was categorized as “unsatisfied”. There were no differences in sex distribution, alcohol consumption, BMI, cholesterol level, hypertension status or education level among participants in each life satisfaction category. But those participants that were unsatisfied were younger, suffered more often from depressed mood, sleep disturbances, life events, had lower SNI, were more often current smokers and physically inactive. In our sample, we tested the association between the dichotomous LS and the CES-D score with logistic regression analysis and was only moderate (OR=0.9, CI=0.8 ; 0.9 in a crude model and OR= 0.8, CI=0.8 – 0.8 in an age and sex-adjusted model).

Covariates

Covariates known to affect sleep quality (outcome), that were also associated with either depressive symptoms or LS (exposures of interest) were identified from the literature[14-18] and discussed prior to the analyses. Socio-demographic variables: age, sex and socioeconomic status were obtained at baseline. Education was used as a proxy for the socio-economic status, classified in years of formal education according to the “International Standard Classification of Education” combining school and vocational training. Four categories were defined with the highest category of 18 and more years of education (equivalent to a University degree), category 3 with 14 to 17 years, category 2 with 11 to 13 years and the lowest category of 10 and less years (equivalent to a basic school degree and no vocational training). Anthropometric measurements (weight and height, body mass index (BMI)=kg/m^2) and blood pressure were determined at the clinical examination. Lifestyle factors were determined through personal interview (alcohol consumption and smoking

habits). Social support, physical activity and life events were determined in the standardized interview. Social support was characterized with the Berkman-Syme's Social Network Index.[38] The components of the index are weighted in an algorithm resulting in four categories (I: low, II: mid-low, III: mid-high, IV: high). Physical activity was assessed by asking participants about the kind and duration of exercise performed in the preceding month, whereby 'physically inactive' meant having performed no exercise at all.[39] In the self-administered questionnaire participants were asked to report whether any stressful life events had occurred in the past 6 months, to which they could answer yes or no. Self-rated health was assessed in the interview by one question ('How would you, referring to the last twelve months, describe your overall health status?') on a 5-point Likert-scale ('very good', 'good', 'moderate', 'poor' and 'very poor').

Statistical Methods

The present study includes only the 3,880 participants at follow-up (89% of the follow-up participants) who filled in the questionnaire. We identified minimally sufficient adjustment sets using diagrams that represent the relations among the exposure, outcome, and other variables.[40] All previously mentioned covariates were considered potential adjustment variables for the relation of LS and depressive symptoms with sleep quality. The minimally sufficient adjustment set for the association of LS and sleep quality included age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, modified CES-D, social support, life events, and physical activity. The minimally sufficient adjustment set for the association of depressive symptoms and sleep quality included age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, LS, social support, life events, and physical activity.

We used multivariable logistic regression to estimate PORs (prevalence odds ratio) that account for depressive symptoms and LS on sleep quality. Exposures were analyzed dichotomously (CES-D score ≥16 vs. < 16 and LS=very satisfied vs. not very satisfied) and continuously (depressive symptoms per 5 unit increase, previously reported as clinically relevant) or categorically (LS 3 categories).[41] Seven hundred twenty two of 3,880 (19%) subjects had missing data for sleep quality, depressive symptoms, LS or covariates. To manage missing data we undertook multiple imputation, using the MI procedure in SAS. We generated an imputed database containing 20 imputed versions using all relevant variables predicting missingness (PSQI score, life satisfaction, CES-D score, age, alcohol consumption, BMI, blood pressure, cholesterol level, life events, sport index score, sex, smoking status, SNI and education level). Regression results were combined using the MIANALYZE procedure in SAS. We explored the pattern of missing data and performed sensitivity analyses on complete cases. Furthermore, we studied the presence of interaction (relative excess risk due to interaction [RERI]) between depressive symptoms and LS by comparing the joint effects of exposure to both factors with the sum of their independent effects. The estimated RERI was calculated as follows:[42]

$$RERI = OR_{11} - OR_{10} - OR_{01} + 1$$

where OR_{11} denotes OR among those exposed to both factors (depressive symptoms and low LS). A RERI of 0 means no interaction, a RERI > 1 means interaction without

monotonicity assumption for one exposure and a RERI > 2 means interaction even without monotonicity assumption for both exposures.[42 43] We performed several sensitivity analyses with the complete case dataset (N=3158). In the first sensitivity analysis, we assumed that both depressive symptoms and sleep quality are strongly sex-dependent, therefore we did sex-stratified interaction analysis to investigate sex-specific patterns. In the second analysis, a higher cut-off for the depression scale (CES-D) was chosen, in order to investigate the robustness of our results. In a third analysis, exposures were treated as continuous (depressive symptoms) or categorical (LS) variables. We have calculated and reported confidence intervals to assess the precision of our estimates because our goal is the estimation and not significance testing. We wish to avoid publication bias by preferential reporting of significant results. Instead, we judge the value of our estimates by their precision and validity. All analyses were performed using SAS 9.3. (SAS Inc., Cary, NC).

RESULTS

Sample characteristics

A total of 1,932 participants (50%) were classified in the "good sleep quality" group which consisted of 57% men with a mean age of 64.4 years (SD 7.5, 51 to 81 years). A total of 1,477 participants (38%) were classified in the “sleep disturbances” category which was 38% male with a mean age of 65.3 years (SD 7.6). A further 471 participants (12%) did not answer the PSQI questionnaire. Table 1 shows demographic and clinical characteristics of participants stratified by sleep quality. Most clinical risk factors (age, hypertension, BMI, cholesterol and physical activity) were not different between the index population of “good sleep quality” and the “sleep disturbed” subgroup. On the contrary, most socio-demographic and psychological variables, e.g. educational level, self-rated health, social network index, life events, depressive symptoms and LS, showed different prevalences between subgroups. Additionally, participants in the good sleep quality group were more often men, current or former smokers and consumed more alcohol.

Association of depressive symptoms and life satisfaction with sleep quality

Table 2 presents the POR estimates for sleep quality with depressive symptoms as a continuous variable (data are shown per 5 unit increments in CES-D scale) and LS as a categorical variable. Similar results were obtained with complete case analysis and multiple imputation, thus we report effect estimates from the multiple imputation analyses. For “depressive symptoms” there was a strong association between depressive symptoms (higher scores in CES-D; 5-units increment) and sleep disturbances (POR = 1.7, 95%CI 1.6 ; 1.8). The results of the logistic regression indicate that participants reporting lower LS

(unsatisfied) had an increased prevalence of suffering from sleep disturbances compared with participants reporting higher LS (very satisfied) (POR =1.5, 95%CI 1.1 ; 2.2). The results of the logistic regression with depression and LS dichotomized are presented in supplementary table 1. The results indicate that participants with higher CES-D scores (depressive symptoms; scores ≥ 16) had an increased prevalence of suffering from sleep disturbances than non-depressed participants (POR = 4.8, 95%CI 3.6 ; 4.5). Participants reporting lower LS had an increased prevalence of suffering from sleep disturbances compared with participants reporting higher LS (POR =1.6, 95%CI 1.3 ; 1.8).

Interaction between LS and depressive symptoms on the prevalence of sleep disturbances

The combined effects of depressive symptoms and LS on sleep quality were greater than the sums of the separate estimated effects (table 3 and supplementary table 2). Multiple imputation and complete case analysis yielded very similar results, thus we report here results from multiple imputation. The RERI for depressive symptoms (score ≥ 16 in the CES-D scale) and LS was 3.7 (95%CI=-0.2 ; 7.1), which indicates that because of the interaction between depressive symptoms and LS, the POR is 3.7 times higher than expected from the addition of the separate effects of depressive symptoms and LS alone. Results for complete case analysis were comparable and are presented in supplementary table 2.

Sensitivity analysis

Several sensitivity analyses in the complete case dataset were performed. Sex-stratified interaction analysis produced similar results (RERI = 2.4 [-2.5 ; 7.4] and RERI= 5.5 [-0.4 ; 11.3]

for women and men respectively) (supplementary tables 3 and 4), but have to be interpreted with caution due to the small numbers of participants in some of the categories. The additive interaction obtained with a higher cut-off for the CES-D scale (scores ≥ 18) was RERI = 4.2 (95%CI=-1.9 ; 10.4). We repeated the interaction analysis with depressive symptoms considered continuously (CES-D score 0 to 42, per 5-unit increase) and LS in 3-categories. The results of this logistic regression indicate that participants with higher CES-D scores (score 15-20) had an increased prevalence of suffering from sleep disturbances than participants with lower scores (score 0-5) (POR = 1.9; 95%CI=1.6 ; 2.3). Participants more dissatisfied with life ("not very satisfied") had an increased prevalence of suffering from sleep disturbances compared with participants satisfied with life ("very satisfied") (POR = 1.5; 95%CI=0.6 ; 3.9). Moreover, the RERI for depressive symptoms and LS (assessed by comparing "very satisfied" with "not very satisfied" and a CES-D score of 0 to a score of 16) was 5.4 (95%CI=-10.0 ; 20.8) (data not shown).

DISCUSSION

Findings from the current study showed that both depressive symptoms and LS were notably associated with sleep quality, emphasizing the importance of both stable and dynamic features of mood on sleep patterns. In agreement with previous studies, we found a negative relation between sleep and depressive symptoms [14] and an overall positive relation between good sleep quality and LS.[15-18] Furthermore, our results suggested that these relationships were best captured by considering the joint effects of depressive symptoms and LS, with higher depressive symptoms associated with substantially worse sleep quality, especially among individuals with lower LS.

Depressive symptoms and LS were only moderately inversely related in our population. This confirms previous literature reporting that they are distinct constructs.[13] [44] Sleep disturbances are part of the diagnostic criteria for depression in ICD-10 and DSM-IV; therefore it is not surprising that CES-D and PSQI scores are so strongly associated. A number of previous studies have shown that depressive symptoms are related to poorer sleep in the adult population with OR of 1.5 to 3.0 in most studies.[2] [45] Our results showed a higher POR for depressive symptoms (4.8, 95%CI 3.6 ; 6.5), probably due to the relatively high cut-off chosen in this study. Additionally, the OR for LS was similar to those previously reported, between 1.8 and 2.1 (POR=1.6, 95%CI=1.3 ; 1.8).[46] [47] Although in concordance with those findings, the present results extend them in several important ways. Most notably, our study examined interaction effects of LS and depressive symptoms on sleep quality.

Ong et al. examined a similar interaction, however only on the multiplicative scale in which they showed that well-being interacts with negative reactivity on overall sleep quality.[17] These results were expanded on the additive scale in our study. The additive interaction analysis examined whether the relative detriment of depressive symptoms on sleep quality was the same across LS groups. We found that participants with depressive symptoms had much worse sleep quality if they belonged to the non-satisfied group than if they belonged to the satisfied group (multiplicative interaction POR = 1.5, 95%CI= 0.6 ; 3.6). However, from a public health perspective, additive interaction is the relevant one, as it can help determine which subgroups would benefit most from a given treatment, i.e. psychotherapy to improve depressive symptoms and thus sleep quality in those participants with low LS. The additive interaction (RERI=3.7, 95%CI=-0.2 ; 7.1) indicates that there is a synergistic effect between depressive symptoms and LS, which substantially increased the prevalence of worse sleep quality. Our study suggests that the depressive symptoms-sleep quality association was modified by LS level in additive interaction analyses.

This study draws its strength from its size and from the fact that it is a population-based sample with well-defined health outcomes and inclusion of an exhaustive list of relevant covariates. Nevertheless, our conclusions are limited by several factors. Our sample consisted of adults with a restricted age range (51 - 81 years) and as with any cross-sectional design, the directionality of the observed associations cannot be determined. Given the age range of the study participants, it is possible that our results cannot be generalised to the complete age range of adults. Women in the post-menopausal period suffer more often than younger and older women from sleep disturbances, depressive symptoms and/or pain. Also men in this age range can present more often pain symptoms. Regarding the

representability of this study population, it has been previously reported that high social class and good health status were overrepresented at baseline of the Heinz Nixdorf Recall Study.[28] Moreover, we used a modified version of the CES-D scale to measure depressive symptoms. Because of this modification, we could not consider previously validated cut-offs for our population. Therefore, we ran sensitivity analyses with various cut-offs (16 and 18) in order to identify relevant changes. In the present study, we did not use sex-specific cut-offs to detect depressive symptoms as previously described in the literature.[48] However, it has been recently reported that several depression tests (Beck Depression Inventory - II, Inventory of Depressive Symptoms - self-report and the Montgomery-Asberg Depression Rating Scale) should use different cut-offs for men and women to better discriminate between depressed and non-depressed participants. Yet, they also affirm that it is too early to recommend gender specific reference values for those tests and that previous studies have found no sex differences for depression scales.[49] Our assessment of LS with a single-item question was limited; however, a recent study has shown that single-item life satisfaction measures performed very similarly compared to the multiple-item SWLS, a more psychometrically established measure.[37] Also, outcome and predictors (sleep quality, depressive symptoms and LS) have been analyzed as dichotomous variables, though they were documented as continuous. Nevertheless, we ran sensitivity analyses with continuous (depressive symptoms) and categorical (LS) exposure variables in complete case analysis in order to identify relevant changes. Finally, the RECALL study was not powered for this research question; therefore some estimates are very imprecise.

These results extend the study of depressive symptoms, LS and sleep quality and suggest that the association between depressive symptoms and sleep quality is modified by LS.

Understanding the predictors of poor sleep quality may have important implications for future health outcomes, such as development of chronic medical conditions.

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Table 1. Demographic and clinical characteristics of participants stratified by sleep quality.

Data are presented as n (%) unless otherwise stated.

			Sleep quality	
Variable		**Total**	**Good [a] (N = 1932)**	**Poor [b] (N = 1477)**
Sex	Women: n (%, CI)	1746	823 (42.6: 40.4 – 44.8)	923 (62.5: 60.0 – 65.0)
	Men: n (%, CI)	1663	1109 (57.4: 55.2 – 59.6)	554 (37.5: 35.0 – 40.0)
Education	< 10 years: n (%, CI)	324	140 (7.3: 6.1 – 8.4)	184 (12.5: 10.8 – 14.1)
	11 – 13 years: n (%, CI)	1910	1005 (52.0: 49.8 – 54.2)	905 (61.3: 58.8 – 63.8)
	14 – 17 years: n (%, CI)	791	531 (27.5: 25.5 – 29.5)	260 (17.6: 15.7 – 19.5)
	≥ 18 years: n (%, CI)	384	256 (13.3: 11.7 – 14.8)	128 (8.7: 7.2 – 10.1)
Smoking	Never smoker: n (%, CI)	1392	731 (39.0: 36.7 – 41.2)	661 (46.7: 44.1 – 49.3)
	Former smoker: n (%, CI)	1343	809 (43.1: 40.9 – 45.3)	534 (37.7: 35.2 – 40.2)
	Current smoker: n (%, CI)	558	337 (18.0: 16.2 – 19.7)	221 (15.6: 13.7 – 17.5)
Self-rated health	Very good: n (%, CI)	164	137 (7.3: 6.1 – 8.5)	27 (1.9: 1.2 – 2.6)
	Good: n (%, CI)	1314	922 (49.2: 46.9 – 51.4)	392 (27.7: 25.4 – 30.0)
	Fair: n (%, CI)	1275	645 (34.4: 32.2 – 36.5)	630 (44.5: 41.9 – 47.1)
	Poor: n (%, CI)	446	137 (7.3: 6.1 – 8.5)	309 (21.8: 19.7 – 24.0)
	Very poor: n (%, CI)	93	35 (1.9: 1.3 – 2.5)	58 (4.1: 3.1 – 5.1)
Social network index	I (low): n (%, CI)	856	443 (23.7: 21.8 – 25.6)	413 (29.2: 26.8 – 31.6)
	II: n (%, CI)	1254	715 (38.2: 36.0 – 40.4)	539 (38.1: 35.6 – 40.7)
	III: n (%, CI)	942	567 (30.3: 28.2 – 32.4)	375 (26.5: 24.2 – 28.8)
	IV (high): n (%, CI)	232	145 (7.8: 6.5 – 9.0)	87 (6.2: 4.9 – 7.4)
Hypertension [c]	Yes: n (%, CI)	1250	755 (40.4: 38.2 – 42.6)	495 (35.1: 32.6 – 37.6)
Physical activity	Active: n (%, CI)	1504	816 (43.5: 41.2 – 45.7)	688 (48.6: 46.0 – 51.2)
Life events in last 6 months	Yes: n (%, CI)	695	346 (18.2: 16.5 – 20.0)	349 (24.1: 21.9 – 26.3)
Depressed mood (CES-D ≥ 16) [d]	Yes: n (%, CI)	294	58 (3.1: 2.3 – 3.8)	236 (16.3: 14.4 – 18.3)

			Sleep quality	
Variable		**Total**	**Good [a]** **(N = 1932)**	**Poor [b]** **(N = 1477)**
Life satisfaction	Very satisfied: n (%, CI)	1194	778 (41.2: 39.0 – 43.4)	416 (28.9: 26.5 – 31.2)
	Quite satisfied: n (%, CI)	1943	1045 (55.4: 53.1 – 57.6)	898 (62.3: 59.8 – 64.8)
	Unsatisfied: n (%, CI)	192	65 (3.4: 2.6 – 4.3)	127 (8.8: 7.3 – 10.3)
Depressed mood: mean (SD) [d]		3338	5.3 (4.4)	9.5 (6.7)
Age years: mean (SD)		3409	64.4 (7.5)	65.3 (7.6)
BMI (kg /m^2) : mean (SD)		3287	28.1 (4.6)	28.3 (5.1)
Total Cholesterol mg/ dL: median (Q1;Q3)		3274	226 (199; 254)	223 (199; 249)
HDL Cholesterol mg/dL: median (Q1;Q3)		3274	59 (49; 71)	57 (48; 69)
Alcohol consumption ml/week: mean (SD)		3306	70.2 (102.7)	57.8 (107.6)

PSQI=Pittsburgh sleep quality index, CES-D= center for epidemiological studies depression scale, BMI=body mass index, HDL=high density lipoprotein. [a] Good sleep quality: PSQI score ≤ 5. [b] Poor sleep quality: PSQI score > 5. [c] Participants on antihypertensive medication or with systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg were defined as hypertensive. [d] CES-D scale excludes the item “my sleep was restless

Table 2. Association of depressed mood and life satisfaction with sleep quality. PORs per 5 unit increment in CES-D scale (depressed mood).

		Complete case analysis		Multiple imputation	
Model	**Adjusted for:**	**N**	**POR (95%CI)**	**N**	**POR (95%CI)**
Depressed mood (score 0 – 42; unit increment=5)					
1	-	3338	2.0 (1.8 – 2.1)	3880	1.8 (1.7 – 1.9)
2	Age and sex	3338	1.9 (1.8 – 2.1)	3880	1.8 (1.6 – 1.9)
3	Fully adjusted [a]	3163	1.8 (1.7 – 2.0)	3880	1.7 (1.6 – 1.8)
Life satisfaction (very -, quite satisfied, unsatisfied)					
1	-	3329		3880	
	Very vs. unsatisfied		3.7 (2.6 – 5.0)		3.6 (2.6 – 4.9)
	Quite vs. unsatisfied		2.3 (1.7 – 3.1)		2.3 (1.7 – 3.1)
2	Age and sex	3329		3880	
	Very vs. unsatisfied		4.2 (3.0 – 5.8)		4.2 (3.0 – 5.7)
	Quite vs. unsatisfied		2.4 (1.7 – 3.2)		2.4 (1.7 – 3.3)
3	Fully adjusted [b]	3163		3880	
	Very vs. unsatisfied		1.5 (1.0 – 2.2)		1.5 (1.1 – 2.2)
	Quite vs. unsatisfied		1.2 (0.9 – 1.8)		1.3 (0.9 – 1.8)

POR=prevalence odds ratio, CI=confidence interval.

[a] Fully adjusted: age, sex, alcohol consumption, BMI (body mass index), blood pressure, total cholesterol, life satisfaction, life events, physical activity, education years, smoking and social support

[b] Fully adjusted: age, sex, alcohol consumption, BMI (body mass index), blood pressure, total cholesterol, CES-D score (center for epidemiological studies depression scale), life events, physical activity, education years, smoking and social support

Table 3. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems (multiple imputation, N=3880)

	Life satisfaction	
	very satisfied	not very satisfied
	POR (95% CI)	POR (95% CI)
Non-depressed mood (cut-off < 16)	1.0	1.5 (1.3 ; 1.8)
Depressed mood (cut-off ≥ 16)	3.4 (1.5 ; 7.9)	7.4 (3.5 ; 11.3)

POR=prevalence odds ratio, CI=confidence interval.

Measure of interaction on additive scale: RERI (95% CI) = 3.7 (-0.2 ; 7.1)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

Supplementary table 1. Association of depressed mood and life satisfaction with sleep quality.

		Complete case analysis		Multiple imputation	
Model	**Adjusted for:**	**N**	**POR (95%CI)**	**N**	**POR (95%CI)**
Depressed mood (<16 not depressed vs. ≥ 16 depressed mood (ref.))					
1	-	3338	6.2 (4.6 – 8.3)	3880	6.4 (4.8 – 8.5)
2	Age and sex	3338	5.8 (4.3 – 7.9)	3880	6.0 (4.5 – 8.0)
3	Age, sex, alcohol consumption, BMI, blood pressure, total cholesterol, life satisfaction, life events, physical activity, education years, smoking and social support	3158	4.6 (3.3 – 6.3)	3880	4.8 (3.6 – 4.5)
Life satisfaction (very satisfied vs. not very satisfied (ref.))					
1	-	3329	1.7 (1.5 – 2.0)	3880	1.7 (1.5 – 1.9)
2	Age and sex	3329	1.9 (1.6 – 2.2)	3880	1.9 (1.6 – 2.2)
3	Age, sex, alcohol consumption, BMI, blood pressure, total cholesterol, CES-D score, life events, physical activity, education years, smoking and social support	3158	1.6 (1.4 – 1.9)	3880	1.6 (1.3 – 1.8)

CES-D= center for epidemiological studies depression scale, BMI=body mass index, POR=prevalence odds ratio, CI=confidence interval.

Supplementary table 2. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems (N=3158)

	Life satisfaction				
	very satisfied		not very satisfied		**POR (95% CI) for life satisfaction within strata of depressed mood**
	N good sleep quality/ N poor sleep quality	POR (95% CI)	N good sleep quality/ N poor sleep quality	POR (95% CI)	
Non-depressed mood (cut-off < 16)	380 / 733	1.0	769 / 1011	1.6 (1.3 ; 1.8)	1.6 (1.3 ; 1.8)
Depressed mood (cut-off ≥ 16)	16 / 7	3.2 (1.3 ; 8.0)	195 / 47	7.3 (5.1 ; 10.4)	2.1 (0.8 ; 5.9)
POR (95% CI) for depressed mood within strata of LS		3.2 (1.3 ; 8.0)		4.2 (3.3 ; 6.6)	

Measure of interaction on additive scale: RERI (95% CI) = 3.6 (-0.2 ; 7.4)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

Supplementary table 3. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems for women (N=1604)

	Life satisfaction				**POR (95% CI) for life satisfaction within strata of depressed mood**
	very satisfied		not very satisfied		
	N sleep problems / no sleep problems	POR (95% CI)	N sleep problems / no sleep problems	POR (95% CI)	
Non-depressed mood (cut-off < 16)	248 / 337	1.0	450 / 396	1.6 (1.3 ; 2.0)	1.6 (1.3 ; 2.0)
Depressed mood (cut-off ≥ 16)	13 / 4	3.6 (1.1 ; 11.3)	130 / 26	6.6 (4.1 ; 10.5)	1.8 (0.4 ; 7.5)
POR (95% CI) for depressed mood within strata of LS		3.6 (1.1 ; 11.3)		4.2 (2.7 ; 6.7)	

Measure of interaction on additive scale: RERI (95% CI) = 2.4 (-2.5 ; 7.4)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

Supplementary table 4. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems for men (N=1554)

	Life satisfaction				**POR (95% CI) for life satisfaction within strata of depressed mood**
	very satisfied		not very satisfied		
	N sleep problems / no sleep problems	POR (95% CI)	N sleep problems / no sleep problems	POR (95% CI)	
Non-depressed mood (cut-off < 16)	132 / 396	1.0	319 / 615	1.5 (1.2 ; 2.0)	1.5 (1.2 ; 2.0)
Depressed mood (cut-off ≥ 16)	3 / 3	2.4 (0.5 ; 12.4)	65 / 21	8.4 (4.9 ; 14.5)	5.5 (0.6 ; 47.5)
POR (95% CI) for depressed mood within strata of LS		2.4 (0.5 ; 12.4)		5.4 (3.2 ; 9.1)	

Measure of interaction on additive scale: RERI (95% CI) = 5.5 (-0.4 ; 11.3)

Measure of interaction on multiplicative scale: ratio of PORs (95% CI) = 2.3 (0.4 ; 12.6)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Depressive symptoms, life satisfaction, and prevalence of sleep disturbances in the general population of Germany. Results from the Heinz Nixdorf Recall Study.

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Running head: depression and life satisfaction synergy on sleep

Keywords: depressive symptoms, life satisfaction, sleep quality, interaction

Word count: 46 references, 3726 main text, 3 tables, 4 supplementary tables

Abstract

Objectives: It appears that not only depression, but also low life satisfaction (LS) is related to sleep complaints in the general population. We evaluate whether the prevalence of sleep complaints attributable to depressed mood is greater among participants with low LS.

Setting, participants and outcome measures: Analysis of cross-sectional data from 3,880 cohort members from the German Heinz Nixdorf Recall study (2006-2008) aged 51 to 81 years. Standard mood (Center for Epidemiological Studies Depression scale (CES-D) for Depressive symptoms and a single-item life satisfaction measure) and sleep quality (Pittsburgh Sleep Quality Index, PSQI) measures were conducted as part of the survey. Multiple imputation was used to deal with missing data in outcome, exposures or covariates. Relative excess risk for interaction (RERI) and its 95% confidence intervals (CIs) were estimated using adjusted prevalence odds ratios. Due to the study size, is the precision of the measures of additive interaction relatively low.

Results: We observed an association between depressed mood (5-units increase in CES-D score) (POR=1.7 [95%CI = 1.6 ; 1.8]) and sleep complaints and between low LS (not very satisfied vs. very satisfied) (POR=1.5 [1.1 ; 2.2]) and sleep complaints. Also, we observed a synergistic effect between lower level of LS (not very satisfied) and depressed mood (score ≥ 16) on prevalence of sleep disorders (RERI = 3.7 [-0.2 ; 7.1]). Furthermore, these findings were corroborated in sensitivity analysis done with the complete case dataset and in sex-specific analyses (RERI = 5.5 [-0.4 ; 11.3] and RERI = 2.4 [-2.5 ; 7.4] for men and women, respectively).

Conclusions: Both depressed mood and LS are notably associated with sleep quality and these relationships are best captured by considering their joint effects. Depression and LS need to be taken in consideration when analyzing sleep quality.

Strengths and limitations

- Strengths: this study draws its strength from its size and from the fact that it is a population-based sample, with well-defined health outcomes, and inclusion of an exhaustive list of relevant covariates.
- Limitations: our sample consisted of adults with a restricted age range (51 - 81 years) and as with any cross-sectional design, the directionality of the observed associations cannot be determined. The precision of our measures of additive interaction (RERI) was quite low because of the sample size.

INTRODUCTION

Sleep is an important source of general health and well-being.[1] Sleep disturbances have been associated with health problems, including poor self-rated health, psychological conditions, chronic medical conditions, and mortality.[2] The prevalence of sleep disturbances in the population is dependent on its definition, and it ranges from 6% (clinical diagnosis of insomnia) to 48% (difficulties in initiating or maintaining sleep or early morning awakening).[3] Considering its high prevalence and association with health conditions, there is a need to investigate the factors associated with sleep disturbances in order to develop strategies to prevent or delay its onset.

Depressive symptomatology is an affective disorder in which the prevailing emotional mood of a person is negatively distorted or inappropriate to the circumstances and is sustained over a particular period of time.[4] Depressive symptoms are considered an important risk factor for insomnia and conversely, sleep disturbances are very common (60-80% prevalence) among depressed patients.[2] In patients with depressive symptoms, insomnia appears either previously (40%) or simultaneously (22%) with other psychological, physical and social symptoms.[5] Following the International Classification of Disease, tenth revision (ICD-X) definition, sleep disturbances are very clearly a symptom of depression, and do not precede it. But sleep complaints are a predictor for depressive relapse if they are a residual symptom after remission.[6] Though, a recent meta-analysis has shown that sleep disturbances can also lead to depression.[7] Also, in a recent systematic review of 9 cohort studies (8 longitudinal and 1 retrospective), the available evidence suggested that sleep disturbances and depression were bidirectionally associated.[8]

Life satisfaction (LS), is a component of subjective well-being.[6] It refers to cognitive judgments that remain quite constant even over a longer period of time.[9 10] A review revealed that subjective well-being, and not only the absence of mental illness, has an effect on all-cause morbidity and mortality.[11] In addition, LS is related to health predictors such as favorable self-reported health, social support, and positive health behaviors.[12] Several studies have shown moderate correlations between life satisfaction (LS) and depressive symptoms, and support independency indicating that research on indicators of well-being adds a distinctive dimension to psychiatric research.[13]

While there are numerous studies associating depression with poor sleep quality (for a review see [14]), there have been fewer studies evaluating associations of well-being and sleep quality. Cross-sectional studies have shown that lower well-being is associated with lower sleep quality.[15-17] Additionally these associations appear to be independent of psychological stressors.[18] It would therefore appear that not only depression is associated with sleep quality, but also well-being, on its own, is associated with sleep quality in the general population. Previous research has shown that depressive symptoms, a transitional period of low mood (state), are associated with worse sleep quality.[19] However, it has not yet been investigated whether well-being, which tends to be stable over time (trait), can alter that association. Recent research has shown that the relationship of mood and sleep quality is best captured by considering the joint effects of both stable and unstable aspects of mood.[17]

There is some support for the assumption that different levels of LS might differentially affect the association between depressive symptomatology and sleep quality. Several studies have shown that resilience, the ability to prosper despite stress and adversity is

associated with LS,[20 21] or that even it can foster LS.[22 23] Moreover, resilience has been associated with better health outcomes in the face of stress and adversity.[24 25] Therefore, it can be assumed that, for participants with higher LS (thus more resilient) the depressive symptomatology would have weaker effects on their sleep quality; whereas for participants with lower LS (and thus less resilient), small levels of depressive symptomatology could lead to greater sleep disturbances.

Aims

This study focuses on the association between depressive symptoms and sleep disturbances and whether this association can be modified by LS. The current study aims to extend our understanding of the relationship between depressive symptoms and the presence of sleep disturbances. In particular, using cross-sectional data from the Heinz Nixdorf Recall Study (2006-2008), we assessed the presence of an interaction between depression and LS on sleep quality, by studying whether the joint effect of exposure to both factors was greater than the sum of their independent effects. We hypothesized that: a) depressive symptoms would negatively relate to sleep quality; b) LS would be positively associated with sleep quality and c) LS would modulate the relation between depressive symptoms and sleep quality. While an explanation of this link cannot be advanced in the frame of a cross-sectional study it seems nevertheless justified to examine the hypothesis that LS modifies this association, such that stronger associations of depressive symptoms with sleep quality are observed among adults with lower LS.

MATERIALS AND METHODS

Study population and study sample

Data were derived from the Heinz Nixdorf Recall (Risk Factors, Evaluation of Coronary Calcium and Lifestyle) Study: a cross-sectional analysis of participants in the follow-up survey when sleep quality and mood assessments took place. The design of the study has been previously described in detail.[26] Briefly, during the baseline examination between December 2000 and August 2003, a total of 4,814 subjects aged between 45 and 75 years were recruited from three adjacent cities in the German Ruhr Area: Essen, Bochum, Mülheim/Ruhr.[26 27] The baseline recruitment proportion was 56%.[28] All subjects were invited for re-examination in 2006-2008. Overall, 154 out of 4,814 subjects (3%) died before re-examination, 503 refused examination (10%) leading to a final 5-years follow-up group of 4,157 subjects (87%). Data collection at follow-up was done through standardized interviews, clinical examination, comprehensive laboratory tests and self-administered questionnaires. The Heinz Nixdorf Recall study was approved by the institutional local ethics committee and has therefore been performed in accordance with the ethical standards laid out in the 1964 Declaration of Helsinki and its later amendments. An internal and external quality management system was established according to industrial standard norms DIN ISO 9001:2000/2008. All participants gave written informed consent.

Outcome

Sleep quality and sleep disturbances in the past month were measured through the Pittsburgh sleep quality index (PSQI).[29] The 19 self-rated items are combined to form seven

component scores, each of which has a range of 0-3 points. A score of "0" indicates no difficulty, while a score of "3" indicates severe difficulties. The seven component scores are then added to yield one "global" score, with a range of 0-21 points, "0" indicating no difficulty and "21" indicating severe sleep disturbances. For the purposes of our study, we examined the PSQI global score, which was calculated using the algorithm outlined in Buysse et al., where a PSQI global score greater than 5 was classified as poor quality sleep.[29]

Major exposures

Depressive symptoms last week was assessed by self-administered questionnaire through the 15 items Center for Epidemiologic Studies Depression scale (CES-D 15).[30 31] We modified the CES-D scale by excluding the symptom "my sleep was restless" to remove the item's correlation with questions on sleep disturbances.[32] Thus, the scale had 14 items and a score range 0 to 42, with higher scores indicative of more symptomatology. A cut-off of 18 has been suggested for depressive symptoms screening in the German population.[33] Because of the removal of an item we considered various cutoffs for depressive symptoms (16 and 18).

LS was measured by self-administered questionnaire through the following question: "how satisfied are you with your personal life?" Answer categories were: very satisfied; usually satisfied; unsatisfied.[34 35] The item-total correlation of this question with the items of the Satisfaction With Life Scale (SWLS) has been reported to be 0.75.[36] Additionally, recent studies have shown that similar single-item LS measures showed a good criterion validity with the SWLS (r=0.62).[37] For analysis purposes we dichotomized this item in "very satisfied"

vs. “not very satisfied”, because only 6% of the population was categorized as “unsatisfied”. There were no differences in sex distribution, alcohol consumption, BMI, cholesterol level, hypertension status or education level among participants in each life satisfaction category. But those participants that were unsatisfied were younger, suffered more often from depressed mood, sleep disturbances, life events, had lower SNI, were more often current smokers and physically inactive. In our sample, we tested the association between the dichotomous LS and the CES-D score with logistic regression analysis and was only moderate (OR=0.9, CI=0.8 ; 0.9 in a crude model and OR= 0.8, CI=0.8 – 0.8 in an age and sex-adjusted model).

Covariates

Covariates known to affect sleep quality (outcome), that were also associated with either depressive symptoms or LS (exposures of interest) were identified from the literature[14-18] and discussed prior to the analyses. Socio-demographic variables: age, sex and socioeconomic status were obtained at baseline. Education was used as a proxy for the socio-economic status, classified in years of formal education according to the “International Standard Classification of Education” combining school and vocational training. Four categories were defined with the highest category of 18 and more years of education (equivalent to a University degree), category 3 with 14 to 17 years, category 2 with 11 to 13 years and the lowest category of 10 and less years (equivalent to a basic school degree and no vocational training). Anthropometric measurements (weight and height, body mass index (BMI)=kg/m^2) and blood pressure were determined at the clinical examination. Lifestyle factors were determined through personal interview (alcohol consumption and smoking

habits). Social support, physical activity and life events were determined in the standardized interview. Social support was characterized with the Berkman-Syme's Social Network Index.[38] The components of the index are weighted in an algorithm resulting in four categories (I: low, II: mid-low, III: mid-high, IV: high). Physical activity was assessed by asking participants about the kind and duration of exercise performed in the preceding month, whereby 'physically inactive' meant having performed no exercise at all.[39] In the self-administered questionnaire participants were asked to report whether any stressful life events had occurred in the past 6 months, to which they could answer yes or no. Self-rated health was assessed in the interview by one question ('How would you, referring to the last twelve months, describe your overall health status?') on a 5-point Likert-scale ('very good', 'good', 'moderate', 'poor' and 'very poor').

Statistical Methods

The present study includes only the 3,880 participants at follow-up (89% of the follow-up participants) who filled in the questionnaire. We identified minimally sufficient adjustment sets using diagrams that represent the relations among the exposure, outcome, and other variables.[40] All previously mentioned covariates were considered potential adjustment variables for the relation of LS and depressive symptoms with sleep quality. The minimally sufficient adjustment set for the association of LS and sleep quality included age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, modified CES-D, social support, life events, and physical activity. The minimally sufficient adjustment set for the association of depressive symptoms and sleep quality included age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, LS, social support, life events, and physical activity.

We used multivariable logistic regression to estimate PORs (prevalence odds ratio) that account for depressive symptoms and LS on sleep quality. Exposures were analyzed dichotomously (CES-D score ≥16 vs. < 16 and LS=very satisfied vs. not very satisfied) and continuously (depressive symptoms per 5 unit increase, previously reported as clinically relevant) or categorically (LS 3 categories).[41] Seven hundred twenty two of 3,880 (19%) subjects had missing data for sleep quality, depressive symptoms, LS or covariates. To manage missing data we undertook multiple imputation, using the MI procedure in SAS. We generated an imputed database containing 20 imputed versions using all relevant variables predicting missingness (PSQI score, life satisfaction, CES-D score, age, alcohol consumption, BMI, blood pressure, cholesterol level, life events, sport index score, sex, smoking status, SNI and education level). Regression results were combined using the MIANALYZE procedure in SAS. We explored the pattern of missing data and performed sensitivity analyses on complete cases. Furthermore, we studied the presence of interaction (relative excess risk due to interaction [RERI]) between depressive symptoms and LS by comparing the joint effects of exposure to both factors with the sum of their independent effects. The estimated RERI was calculated as follows:[42]

$$RERI = OR_{11} - OR_{10} - OR_{01} + 1$$

where OR_{11} denotes OR among those exposed to both factors (depressive symptoms and low LS). A RERI of 0 means no interaction, a RERI > 1 means interaction without

monotonicity assumption for one exposure and a RERI > 2 means interaction even without monotonicity assumption for both exposures.[42 43] We performed several sensitivity analyses with the complete case dataset (N=3158). In the first sensitivity analysis, we assumed that both depressive symptoms and sleep quality are strongly sex-dependent, therefore we did sex-stratified interaction analysis to investigate sex-specific patterns. In the second analysis, a higher cut-off for the depression scale (CES-D) was chosen, in order to investigate the robustness of our results. In a third analysis, exposures were treated as continuous (depressive symptoms) or categorical (LS) variables. We have calculated and reported confidence intervals to assess the precision of our estimates because our goal is the estimation and not significance testing. We wish to avoid publication bias by preferential reporting of significant results. Instead, we judge the value of our estimates by their precision and validity. All analyses were performed using SAS 9.3. (SAS Inc., Cary, NC).

RESULTS

Sample characteristics

A total of 1,932 participants (50%) were classified in the "good sleep quality" group which consisted of 57% men with a mean age of 64.4 years (SD 7.5, 51 to 81 years). A total of 1,477 participants (38%) were classified in the “sleep disturbances” category which was 38% male with a mean age of 65.3 years (SD 7.6). A further 471 participants (12%) did not answer the PSQI questionnaire. Table 1 shows demographic and clinical characteristics of participants stratified by sleep quality. Most clinical risk factors (age, hypertension, BMI, cholesterol and physical activity) were not different between the index population of “good sleep quality” and the “sleep disturbed” subgroup. On the contrary, most socio-demographic and psychological variables, e.g. educational level, self-rated health, social network index, life events, depressive symptoms and LS, showed different prevalences between subgroups. Additionally, participants in the good sleep quality group were more often men, current or former smokers and consumed more alcohol.

Association of depressive symptoms and life satisfaction with sleep quality

Table 2 presents the POR estimates for sleep quality with depressive symptoms as a continuous variable (data are shown per 5 unit increments in CES-D scale) and LS as a categorical variable. Similar results were obtained with complete case analysis and multiple imputation, thus we report effect estimates from the multiple imputation analyses. For “depressive symptoms” there was a strong association between depressive symptoms (higher scores in CES-D; 5-units increment) and sleep disturbances (POR = 1.7, 95%CI 1.6 ; 1.8). The results of the logistic regression indicate that participants reporting lower LS

(unsatisfied) had an increased prevalence of suffering from sleep disturbances compared with participants reporting higher LS (very satisfied) (POR =1.5, 95%CI 1.1 ; 2.2). The results of the logistic regression with depression and LS dichotomized are presented in supplementary table 1. The results indicate that participants with higher CES-D scores (depressive symptoms; scores ≥ 16) had an increased prevalence of suffering from sleep disturbances than non-depressed participants (POR = 4.8, 95%CI 3.6 ; 4.5). Participants reporting lower LS had an increased prevalence of suffering from sleep disturbances compared with participants reporting higher LS (POR =1.6, 95%CI 1.3 ; 1.8).

Interaction between LS and depressive symptoms on the prevalence of sleep disturbances

The combined effects of depressive symptoms and LS on sleep quality were greater than the sums of the separate estimated effects (table 3 and supplementary table 2). Multiple imputation and complete case analysis yielded very similar results, thus we report here results from multiple imputation. The RERI for depressive symptoms (score ≥ 16 in the CES-D scale) and LS was 3.7 (95%CI=-0.2 ; 7.1), which indicates that because of the interaction between depressive symptoms and LS, the POR is 3.7 times higher than expected from the addition of the separate effects of depressive symptoms and LS alone. Results for complete case analysis were comparable and are presented in supplementary table 2.

Sensitivity analysis

Several sensitivity analyses in the complete case dataset were performed. Sex-stratified interaction analysis produced similar results (RERI = 2.4 [-2.5 ; 7.4] and RERI= 5.5 [-0.4 ; 11.3]

for women and men respectively) (supplementary tables 3 and 4), but have to be interpreted with caution due to the small numbers of participants in some of the categories. The additive interaction obtained with a higher cut-off for the CES-D scale (scores ≥ 18) was RERI = 4.2 (95%CI=-1.9 ; 10.4). We repeated the interaction analysis with depressive symptoms considered continuously (CES-D score 0 to 42, per 5-unit increase) and LS in 3-categories. The results of this logistic regression indicate that participants with higher CES-D scores (score 15-20) had an increased prevalence of suffering from sleep disturbances than participants with lower scores (score 0-5) (POR = 1.9; 95%CI=1.6 ; 2.3). Participants more dissatisfied with life ("not very satisfied") had an increased prevalence of suffering from sleep disturbances compared with participants satisfied with life ("very satisfied") (POR = 1.5; 95%CI=0.6 ; 3.9). Moreover, the RERI for depressive symptoms and LS (assessed by comparing "very satisfied" with "not very satisfied" and a CES-D score of 0 to a score of 16) was 5.4 (95%CI=-10.0 ; 20.8) (data not shown).

DISCUSSION

Findings from the current study showed that both depressive symptoms and LS were notably associated with sleep quality, emphasizing the importance of both stable and dynamic features of mood on sleep patterns. In agreement with previous studies, we found a negative relation between sleep and depressive symptoms [14] and an overall positive relation between good sleep quality and LS.[15-18] Furthermore, our results suggested that these relationships were best captured by considering the joint effects of depressive symptoms and LS, with higher depressive symptoms associated with substantially worse sleep quality, especially among individuals with lower LS.

Depressive symptoms and LS were only moderately inversely related in our population. This confirms previous literature reporting that they are distinct constructs.[13 44] Sleep disturbances are part of the diagnostic criteria for depression in ICD-10 and DSM-IV; therefore it is not surprising that CES-D and PSQI scores are so strongly associated. A number of previous studies have shown that depressive symptoms are related to poorer sleep in the adult population with OR of 1.5 to 3.0 in most studies.[2 45] Our results showed a higher POR for depressive symptoms (4.8, 95%CI 3.6 ; 6.5), probably due to the relatively high cut-off chosen in this study. Additionally, the OR for LS was similar to those previously reported, between 1.8 and 2.1 (POR=1.6, 95%CI=1.3 ; 1.8).[46 47] Although in concordance with those findings, the present results extend them in several important ways. Most notably, our study examined interaction effects of LS and depressive symptoms on sleep quality.

Ong et al. examined a similar interaction, however only on the multiplicative scale in which they showed that well-being interacts with negative reactivity on overall sleep quality.[17] These results were expanded on the additive scale in our study. The additive interaction analysis examined whether the relative detriment of depressive symptoms on sleep quality was the same across LS groups. We found that participants with depressive symptoms had much worse sleep quality if they belonged to the non-satisfied group than if they belonged to the satisfied group (multiplicative interaction POR = 1.5, 95%CI= 0.6 ; 3.6). However, from a public health perspective, additive interaction is the relevant one, as it can help determine which subgroups would benefit most from a given treatment, i.e. psychotherapy to improve depressive symptoms and thus sleep quality in those participants with low LS. The additive interaction (RERI=3.7, 95%CI=-0.2 ; 7.1) indicates that there is a synergistic effect between depressive symptoms and LS, which substantially increased the prevalence of worse sleep quality. Our study suggests that the depressive symptoms-sleep quality association was modified by LS level in additive interaction analyses.

This study draws its strength from its size and from the fact that it is a population-based sample with well-defined health outcomes and inclusion of an exhaustive list of relevant covariates. Nevertheless, our conclusions are limited by several factors. Our sample consisted of adults with a restricted age range (51 - 81 years) and as with any cross-sectional design, the directionality of the observed associations cannot be determined. Given the age range of the study participants, it is possible that our results cannot be generalised to the complete age range of adults. Women in the post-menopausal period suffer more often than younger and older women from sleep disturbances, depressive symptoms and/or pain. Also men in this age range can present more often pain symptoms. Regarding the

representability of this study population, it has been previously reported that high social class and good health status were overrepresented at baseline of the Heinz Nixdorf Recall Study.[28] Moreover, we used a modified version of the CES-D scale to measure depressive symptoms. Because of this modification, we could not consider previously validated cut-offs for our population. Therefore, we ran sensitivity analyses with various cut-offs (16 and 18) in order to identify relevant changes. In the present study, we did not use sex-specific cut-offs to detect depressive symptoms as previously described in the literature.[48] However, it has been recently reported that several depression tests (Beck Depression Inventory - II, Inventory of Depressive Symptoms - self-report and the Montgomery-Asberg Depression Rating Scale) should use different cut-offs for men and women to better discriminate between depressed and non-depressed participants. Yet, they also affirm that it is too early to recommend gender specific reference values for those tests and that previous studies have found no sex differences for depression scales.[49] Our assessment of LS with a single-item question was limited; however, a recent study has shown that single-item life satisfaction measures performed very similarly compared to the multiple-item SWLS, a more psychometrically established measure.[37] Also, outcome and predictors (sleep quality, depressive symptoms and LS) have been analyzed as dichotomous variables, though they were documented as continuous. Nevertheless, we ran sensitivity analyses with continuous (depressive symptoms) and categorical (LS) exposure variables in complete case analysis in order to identify relevant changes. Finally, the RECALL study was not powered for this research question; therefore some estimates are very imprecise.

These results extend the study of depressive symptoms, LS and sleep quality and suggest that the association between depressive symptoms and sleep quality is modified by LS.

Understanding the predictors of poor sleep quality may have important implications for future health outcomes, such as development of chronic medical conditions.

Contributor statement: ASP, ND, SM, SD, SM, AS, HK, RE and AS contributed to the study design and data acquisition. AS supervised all aspects of the study's execution. MEL planned the analysis and undertook the primary analysis and wrote the first draft of the paper. All authors critically reviewed the paper and approved the submitted version.

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Table 1. Demographic and clinical characteristics of participants stratified by sleep quality.

Data are presented as n (%) unless otherwise stated.

			Sleep quality	
Variable		**Total**	**Good [a] (N = 1932)**	**Poor [b] (N = 1477)**
Sex	Women: n (%, CI)	1746	823 (42.6: 40.4 – 44.8)	923 (62.5: 60.0 – 65.0)
	Men: n (%, CI)	1663	1109 (57.4: 55.2 – 59.6)	554 (37.5: 35.0 – 40.0)
Education	< 10 years: n (%, CI)	324	140 (7.3: 6.1 – 8.4)	184 (12.5: 10.8 – 14.1)
	11 – 13 years: n (%, CI)	1910	1005 (52.0: 49.8 – 54.2)	905 (61.3: 58.8 – 63.8)
	14 – 17 years: n (%, CI)	791	531 (27.5: 25.5 – 29.5)	260 (17.6: 15.7 – 19.5)
	≥ 18 years: n (%, CI)	384	256 (13.3: 11.7 – 14.8)	128 (8.7: 7.2 – 10.1)
Smoking	Never smoker: n (%, CI)	1392	731 (39.0: 36.7 – 41.2)	661 (46.7: 44.1 – 49.3)
	Former smoker: n (%, CI)	1343	809 (43.1: 40.9 – 45.3)	534 (37.7: 35.2 – 40.2)
	Current smoker: n (%, CI)	558	337 (18.0: 16.2 – 19.7)	221 (15.6: 13.7 – 17.5)
Self-rated health	Very good: n (%, CI)	164	137 (7.3: 6.1 – 8.5)	27 (1.9: 1.2 – 2.6)
	Good: n (%, CI)	1314	922 (49.2: 46.9 – 51.4)	392 (27.7: 25.4 – 30.0)
	Fair: n (%, CI)	1275	645 (34.4: 32.2 – 36.5)	630 (44.5: 41.9 – 47.1)
	Poor: n (%, CI)	446	137 (7.3: 6.1 – 8.5)	309 (21.8: 19.7 – 24.0)
	Very poor: n (%, CI)	93	35 (1.9: 1.3 – 2.5)	58 (4.1: 3.1 – 5.1)
Social network index	I (low): n (%, CI)	856	443 (23.7: 21.8 – 25.6)	413 (29.2: 26.8 – 31.6)
	II: n (%, CI)	1254	715 (38.2: 36.0 – 40.4)	539 (38.1: 35.6 – 40.7)
	III: n (%, CI)	942	567 (30.3: 28.2 – 32.4)	375 (26.5: 24.2 – 28.8)
	IV (high): n (%, CI)	232	145 (7.8: 6.5 – 9.0)	87 (6.2: 4.9 – 7.4)
Hypertension [c]	Yes: n (%, CI)	1250	755 (40.4: 38.2 – 42.6)	495 (35.1: 32.6 – 37.6)
Physical activity	Active: n (%, CI)	1504	816 (43.5: 41.2 – 45.7)	688 (48.6: 46.0 – 51.2)
Life events in last 6 months	Yes: n (%, CI)	695	346 (18.2: 16.5 – 20.0)	349 (24.1: 21.9 – 26.3)
Depressed mood (CES-D ≥ 16) [d]	Yes: n (%, CI)	294	58 (3.1: 2.3 – 3.8)	236 (16.3: 14.4 – 18.3)

			Sleep quality	
Variable		**Total**	**Good [a]** **(N = 1932)**	**Poor [b]** **(N = 1477)**
Life satisfaction	Very satisfied: n (%, CI)	1194	778 (41.2: 39.0 – 43.4)	416 (28.9: 26.5 – 31.2)
	Quite satisfied: n (%, CI)	1943	1045 (55.4: 53.1 – 57.6)	898 (62.3: 59.8 – 64.8)
	Unsatisfied: n (%, CI)	192	65 (3.4: 2.6 – 4.3)	127 (8.8: 7.3 – 10.3)
Depressed mood: mean (SD) [d]		3338	5.3 (4.4)	9.5 (6.7)
Age years: mean (SD)		3409	64.4 (7.5)	65.3 (7.6)
BMI (kg /m^2) : mean (SD)		3287	28.1 (4.6)	28.3 (5.1)
Total Cholesterol mg/ dL: median (Q1;Q3)		3274	226 (199; 254)	223 (199; 249)
HDL Cholesterol mg/dL: median (Q1;Q3)		3274	59 (49; 71)	57 (48; 69)
Alcohol consumption ml/week: mean (SD)		3306	70.2 (102.7)	57.8 (107.6)

PSQI=Pittsburgh sleep quality index, CES-D= center for epidemiological studies depression scale, BMI=body mass index, HDL=high density lipoprotein. [a] Good sleep quality: PSQI score ≤ 5. [b] Poor sleep quality: PSQI score > 5. [c] Participants on antihypertensive medication or with systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg were defined as hypertensive. [d] CES-D scale excludes the item “my sleep was restless

Table 2. Association of depressed mood and life satisfaction with sleep quality. PORs per 5 unit increment in CES-D scale (depressed mood).

		Complete case analysis		Multiple imputation	
Model	**Adjusted for:**	**N**	**POR (95%CI)**	**N**	**POR (95%CI)**
Depressed mood (score 0 – 42; unit increment=5)					
1	-	3338	2.0 (1.8 – 2.1)	3880	1.8 (1.7 – 1.9)
2	Age and sex	3338	1.9 (1.8 – 2.1)	3880	1.8 (1.6 – 1.9)
3	Fully adjusted [a]	3163	1.8 (1.7 – 2.0)	3880	1.7 (1.6 – 1.8)
Life satisfaction (very -, quite satisfied, unsatisfied)					
1	-	3329		3880	
	Very vs. unsatisfied		3.7 (2.6 – 5.0)		3.6 (2.6 – 4.9)
	Quite vs. unsatisfied		2.3 (1.7 – 3.1)		2.3 (1.7 – 3.1)
2	Age and sex	3329		3880	
	Very vs. unsatisfied		4.2 (3.0 – 5.8)		4.2 (3.0 – 5.7)
	Quite vs. unsatisfied		2.4 (1.7 – 3.2)		2.4 (1.7 – 3.3)
3	Fully adjusted [b]	3163		3880	
	Very vs. unsatisfied		1.5 (1.0 – 2.2)		1.5 (1.1 – 2.2)
	Quite vs. unsatisfied		1.2 (0.9 – 1.8)		1.3 (0.9 – 1.8)

POR=prevalence odds ratio, CI=confidence interval.

[a] Fully adjusted: age, sex, alcohol consumption, BMI (body mass index), blood pressure, total cholesterol, life satisfaction, life events, physical activity, education years, smoking and social support

[b] Fully adjusted: age, sex, alcohol consumption, BMI (body mass index), blood pressure, total cholesterol, CES-D score (center for epidemiological studies depression scale), life events, physical activity, education years, smoking and social support

Table 3. Interaction between LS and depressed mood (cut-off ≥ 16) on the prevalence of sleep problems (multiple imputation, N=3880)

	Life satisfaction	
	very satisfied	not very satisfied
	POR (95% CI)	POR (95% CI)
Non-depressed mood (cut-off < 16)	1.0	1.5 (1.3 ; 1.8)
Depressed mood (cut-off ≥ 16)	3.4 (1.5 ; 7.9)	7.4 (3.5 ; 11.3)

POR=prevalence odds ratio, CI=confidence interval.

Measure of interaction on additive scale: RERI (95% CI) = 3.7 (-0.2 ; 7.1)

PORs are adjusted for age, sex, socioeconomic status, smoking, BMI, alcohol consumption, cholesterol, social support, life events, and physical activity.