CME INSTITUTE™

Sleep in Depression and Anxiety Disorders: A Population-Based Study of Elderly Persons

Julia F. van den Berg, PhD; Hendrika J. Luijendijk, MD, MPH; Joke H. M. Tulen, PhD; Albert Hofman, MD, PhD; Arie Knuistingh Neven, MD, PhD; and Henning Tiemeier, MD, PhD

Objective: Sleep disturbance is common in psychiatric disorders. However, the relationships of core parameters in sleep research, such as total sleep time (TST), with depression and anxiety disorders are unclear and have rarely been investigated in large population-based studies.

Method: This study was embedded in the Rotterdam Study, a community-based cohort study of elderly persons living in a district of Rotterdam, The Netherlands. Between January 2002 and December 2005, sleep parameters were assessed with the Pittsburgh Sleep Quality Index in 5,019 persons aged 58 to 100 years. *DSM-IV-TR* diagnoses of depressive and anxiety disorders were ascertained by psychiatric interview (the Schedules for Clinical Assessment in Neuropsychiatry for depressive disorders and a slightly adapted Munich version of the Composite International Diagnostic Interview for anxiety disorders). Associations between sleep parameters and psychiatric disorders were investigated with analyses of covariance and logistic regression models.

Results: Both short-duration (< 6 hours per night) and long-duration (≥ 9 hours per night) sleepers were more likely to have a depressive disorder ($P < .001$) than were those sleeping 7 to < 8 hours per night; the association between TST and anxiety disorders was also U-shaped. These associations were stronger in people who did not use psychoactive medication but did not substantially change after exclusion of persons with probable sleep apnea or excessive alcohol use. Participants with a depressive disorder and a comorbid anxiety disorder reported a 1-hour shorter TST than persons with 1 disorder or no disorders ($P < .001$). On average, however, depressed persons spent more time in bed than did the nondepressed group.

Conclusion: In a community-dwelling older population, not only insomnia or short sleep but also long sleep can be symptomatic of psychiatric disorders such as depression and anxiety disorders.

J Clin Psychiatry 2009;70(8):1105–1113

© Copyright 2009 Physicians Postgraduate Press, Inc.

Submitted: *June 6, 2008; accepted October 8, 2008.*
Online ahead of print: *July 14, 2009 (doi:10.4088/JCP.08m04448).*
Corresponding author: *Henning Tiemeier, MD, PhD, Department of Epidemiology, Erasmus Medical Center, PO Box 2040, 3000 CA Rotterdam, The Netherlands (h.tiemeier@erasmusmc.nl).*

Total sleep time (TST) is a core parameter in clinical sleep medicine and epidemiologic sleep research. It is related to well-being, health, and mortality.[1,2] Individual differences in TST may result from psychiatric disorders, such as depression—because depression is strongly related to sleep disturbance[3–8]: in 40% to 90% of subjects with diagnosed depression, complaints of poor sleep quality are observed.[5,7,8] Some authors have suggested that depression may be involved in the mechanisms explaining the U-shaped curve between sleep duration and mortality, particularly at the "long sleep" tail of the curve.[9] However, others reported that depression did not have a substantial moderating influence on the association of sleep with mortality.[1,10]

The association between depression and sleep disturbance has been extensively studied. Polysomnographic sleep research has shown alterations of sleep architecture in depression, in particular an impaired sleep efficiency, a reduction of slow-wave sleep, and changes in rapid eye movement (REM) sleep.[5,11] Several hypotheses regarding physiologic mechanisms underlying sleep disturbance in depression have been discussed in an elaborate review by Tsuno et al.[5] The association of depression with poor sleep quality has also been studied in epidemiologic research. These studies show that the relationship is bidirectional: on the one hand, depression strongly increases the risk of poor sleep quality, and, on the other hand, poor sleep quality is a predictor for future depressive episodes.[4–6,8,12,13] This relationship holds even after accounting for previous depression.[11] Although the relationship between depression and perceived or measured sleep disturbance is of great clinical interest, from an epidemiologic perspective, other sleep parameters are important as well. Most previous studies that examined associations between mental health and sleep disturbance did not analyze other sleep parameters such as TST, time spent in bed (TIB), or time needed to fall asleep (sleep onset latency [SOL]). The few studies that did investigate the association between TST and depression reported conflicting results. Chang et al[13] found that those getting 7 hours of sleep or less were more likely to develop a depressive disorder than those getting more than 7 hours of sleep, but this association was only marginally significant in an adjusted model. Taylor et al[14] could not detect any

© COPYRIGHT 2009 PHYSICIANS POSTGRADUATE PRESS, INC. © COPYRIGHT 2009 PHYSICIANS POSTGRADUATE PRESS, INC.

For Clinical Use

- In elderly persons, not only short sleep but also long sleep can be symptomatic of psychiatric disorders such as depression and anxiety.
- Clinicians should inquire not only about the number of hours a depressed or anxious person sleeps but also about the time he or she spends in bed.
- The use of psychoactive medication strongly attenuates the relationship between short sleep duration and prevalent depression.

association between TST or SOL and depression or anxiety. Some epidemiologic studies[1,15] found a higher likelihood of depression, or a higher number of depressive symptoms, in both short-duration and long-duration sleepers, defined as either shorter or longer than 7 hours, respectively,[1] or as shorter than 6 hours and longer than 8 hours, respectively.[15] One previous study[2] reported on the association between long sleep (9 or more hours) and depression, but, since long sleep was the focus of this study, they did not report whether a U-shaped curve was present. These differences in observations may be a consequence of differences in assessment methods of both sleep and psychiatric disorders. In most population-based studies, questionnaires are used for the ascertainment of psychiatric disorders; the use of psychiatric interviews is exceptional.

Poor sleep can also be a consequence or symptom of an anxiety disorder.[16–19] It is, for example, an important symptom of generalized anxiety disorder,[17] which is the most common anxiety disorder among older adults.[20] It has also been shown that insomnia is common in patients with panic disorder[19,21] and related to "trait" anxiety.[14] Whereas sleep in depressive disorders has been extensively studied, the study of sleep in anxiety disorders is less well developed. In particular, the relationship between anxiety disorders and sleep parameters has scarcely been studied in population samples. Anxiety disorders frequently coexist with depressive disorders,[22] and this comorbidity may affect sleep even more than having only 1 disorder.

Many previous studies of sleep disturbance and psychiatric disorders were performed in clinical populations or otherwise selected groups, which limits the generalizability of the results.

The present study examined various sleep parameters in 5,019 community-dwelling elderly persons. We were interested in the relationships of sleep parameters (TST, TIB, SOL, and self-reported global sleep quality) with depression and anxiety. As psychiatric disorders are known to be associated with poor sleep, we expected SOL to be longer and sleep quality to be poorer in persons with depressive or anxiety disorders than in persons without these disorders and to be probably even more altered in persons with both disorders. We had no a priori hypothesis about TIB. As both insomnia and hypersomnia can be symptomatic of depressive disorders according to the *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, Text Revision (*DSM-IV-TR*),[23] we hypothesized that both long and short sleep durations are associated with depressive disorders. We defined *short sleep* and *long sleep* as shorter or longer than the reference category of 7 to < 8 hours per night, which was the median sleep duration in our study.

As anxiety disorders are likely to involve increased arousal, we expected an association between short sleep and anxiety disorders but not between long sleep and anxiety disorders. We nevertheless explored whether such a relationship exists, considering the relationship both between TST and anxiety disorders in general and between TST and specific anxiety disorders. To rule out that relationships between TST and psychiatric disorders are explained by the use of psychoactive medication or alcohol and by the presence of sleep apnea, we repeated the analyses after exclusion of these groups. Finally, we tested whether long sleepers and short sleepers with psychiatric disorders were characterized by specific features.

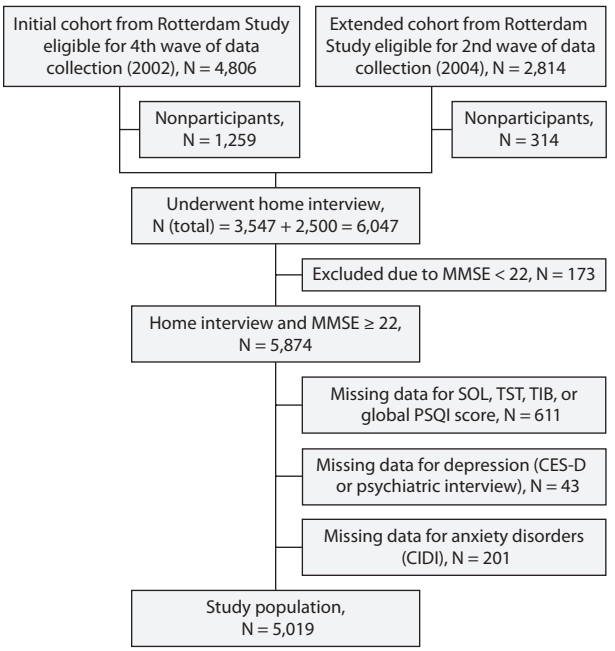
METHOD

Study Population

This study is embedded in the Rotterdam Study, a population-based cohort study aimed at assessing the occurrence of and risk factors for chronic diseases in the elderly.[24] In 1990, all inhabitants of a district of Rotterdam aged 55 years and over were invited to participate. In 2000, the study population was extended with a second cohort of people aged 55 years and over. Between January 2002 and December 2005, 3,547 participants from the original cohort and 2,500 participants from the extended cohort underwent a home interview. Of these 6,047 participants, 173 persons were excluded because of considerable cognitive impairment (Mini-Mental State Examination [MMSE][25] score < 22), as we expected the assessment of both psychiatric disorders and sleep to be unreliable in these persons. For 5,019 of the remaining 5,874 participants, complete and valid data on sleep, depression, and anxiety disorders were available. Figure 1 shows the composition of the study population in a flowchart. The Medical Ethics Committee of Erasmus University Rotterdam approved the Rotterdam

© Copyright 2009 Physicians Postgraduate Press, Inc. © Copyright 2009 Physicians Postgraduate Press, Inc.

Figure 1. Flowchart Showing Composition of the Study Population



Abbreviations: CES-D = Center for Epidemiologic Studies Depression Scale, CIDI = Composite International Diagnostic Interview, MMSE = Mini-Mental State Examination, PSQI = Pittsburgh Sleep Quality Index, SOL = sleep onset latency, TIB = time in bed, TST = total sleep time.

Study, and written informed consent was obtained from all participants.

Assessment of Sleep Parameters

We assessed subjective sleep quality with the Dutch version of the Pittsburgh Sleep Quality Index (PSQI)[26] as a part of the home interview. The PSQI is a self-rated questionnaire that measures sleep quality and disturbance retrospectively over a 1-month period, resulting in a global score between 0 and 21, with higher scores indicating poorer sleep quality. Self-reported TST and SOL were derived from 2 individual PSQI questions. Time in bed was calculated from self-reported bedtime and get-up time.

Assessment of Depression and Anxiety

Depressive disorders were diagnosed using a 2-step procedure. First, participants were screened for depressive symptoms with a validated Dutch translation[27] of the original Center for Epidemiologic Studies Depression Scale (CES-D)[28] by Radloff et al during the home interview. As a second step, subjects with a CES-D score ≥ 16 underwent a semistructured psychiatric interview with the Schedules for Clinical Assessment in Neuropsychiatry[29] (formerly known as Present State Examination) performed by an experienced clinician. Depressive disorders (major depressive disorder, minor depressive disorder, and dysthymic disorder) were classified according to *DSM-IV-TR* criteria.[23] As part of the initial home interview, a slightly adapted Munich version of the Composite International Diagnostic Interview (M-CIDI)[30,31] was administered to assess the following anxiety disorders according to *DSM-IV-TR* criteria[23]: generalized anxiety disorder, specific phobia, social phobia, agoraphobia without panic disorder, and panic disorder with or without history of agoraphobia. As the prevalences of most of the separate disorders were low in our study population, we used 2 dichotomous variables indicating whether or not a person had at least 1 of the *DSM-IV-TR* depressive disorders or 1 of the anxiety disorders. However, generalized anxiety disorder and agoraphobia could also be analyzed separately, as these were the 2 largest groups.

Assessment of Other Variables

The use of psychoactive medication (antidepressants, anxiolytics, sedatives, hypnotics) and alcohol was assessed in the home interview. *Excessive alcohol use* was defined as more than 21 alcoholic drinks per week. Cognitive function was assessed with the MMSE.[25] Scores on this test range from 0 to 30, with higher scores indicating a better cognitive performance. To evaluate functional disability, we used the Stanford Health Assessment Questionnaire,[32] a subjective measure of physical health with emphasis on the ability to perform daily activities in 5 different domains. This instrument has been validated in different populations and is frequently used in studies with normal aging populations.[33] Higher scores on this questionnaire represent more disability. To operationalize the occurrence of probable sleep apnea, 2 questions from the PSQI were used. In line with Fogelholm et al,[34] in our study sleep apnea was considered probable in persons who reported (1) loud snoring at least 2 nights a week, with at least occasional respiratory pauses, or (2) respiratory pauses during sleep with a frequency of at least 1 to 2 nights weekly. All of the questionnaires were administered as part of the home interview.

Statistical Analysis

We divided our study population into 4 groups: persons without any depressive or anxiety disorder (reference group), persons with only a depressive disorder, persons with only an anxiety disorder, and persons with both a depressive disorder and an anxiety disorder. We used analysis of covariance to estimate age- and gender-adjusted mean values of self-reported TST, SOL, TIB, and global PSQI score for each of the groups—and differences from the values of the reference group.

To investigate whether quadratic relationships existed between TST and depressive disorders or anxiety disorders, we performed logistic regression analyses with a continuous measure of TST as the independent variable and depressive disorder and anxiety disorder, respectively, as dichotomous dependent variables. It has to be noted that with neither of our analyses did we imply a causal or temporal direction of

COPYRIGHT 2009 PHYSICIANS POSTGRADUATE PRESS, INC. © COPYRIGHT 2009 PHYSICIANS POSTGRADUATE PRESS, INC.

Table 1. Demographic and Clinical Characteristics of the Study Population

Characteristic	Total Study Population (N = 5,019)	No Depressive Disorder or Anxiety Disorder (n = 4,499)	Depressive Disorder, No Anxiety Disorder (n = 113)	Anxiety Disorder, No Depressive Disorder (n = 341)	Both Depressive Disorder and Anxiety Disorder (n = 66)
Age, mean (SD), y	72.4 (7.6)	72.3 (7.6)	75.3 (8.8)	71.7 (7.2)	73.9 (7.7)
Gender, female, n (%)[a]	2,848 (56.7)	2,453 (54.5)	78 (69.0)	264 (77.4)	53 (80.3)
Cognitive function, MMSE score, mean (SD)[b]	27.7 (1.8)	27.7 (1.8)	27.1 (2.1)	27.5 (1.8)	26.9 (2.0)
Depressive symptoms, CES-D score, mean (SD)	6.0 (7.4)	4.9 (5.7)	24.6 (7.2)	9.6 (9.1)	30.0 (8.4)
Functional disability, HAQ score, mean (SD)	1.5 (0.6)	1.5 (0.5)	2.1 (0.8)	1.7 (0.6)	1.9 (0.7)
Use of psychoactive medication, n (%)[a]	805 (17.2)	613 (14.7)	57 (53.3)	104 (32.1)	31 (50.8)
Excessive alcohol consumption, > 21 drinks per week, n (%)[a]	531 (10.7)	488 (11.0)	13 (11.7)	29 (8.7)	1 (1.5)
Probable sleep apnea, n (%)[a]	403 (10.3)	370 (10.5)	10 (12.7)	21 (8.4)	2 (4.8)

[a]Percentages refer to the cases with information on this variable (valid percentage).
[b]Persons with MMSE score < 22 have been excluded.
Abbreviations: CES-D = Center for Epidemiologic Studies Depression Scale, HAQ = Stanford Health Assessment Questionnaire, MMSE = Mini-Mental State Examination.

Table 2. Depressive Disorders, Anxiety Disorders, and Sleep Parameters in the Study Population (N = 5,019)

Characteristic	Mean (SD)
Sleep parameters	
Total sleep time, h	6.88 (1.27)
Sleep onset latency, min	21.6 (28.8)
Time in bed, h	7.74 (1.10)
Global PSQI score	3.9 (3.6)
	n (%)
DSM-IV-TR depressive disorders (total)[a]	179 (3.6)
Major depressive disorder	98 (2.0)
Minor depressive disorder	62 (1.2)
Dysthymic disorder	19 (0.4)
DSM-IV-TR anxiety disorders (total)[a]	407 (8.1)
Generalized anxiety disorder	111 (2.2)
Social phobia	56 (1.1)
Specific phobia	79 (1.6)
Agoraphobia without history of panic disorder	195 (3.9)
Panic disorder with or without agoraphobia	28 (0.5)

[a]Categories of depressive disorders are mutually exclusive, but categories of anxiety disorders are not.
Abbreviation: PSQI = Pittsburgh Sleep Quality Index.

the associations under study. We tested both linear models and models in which a quadratic term was added since both short and long sleep may be related to psychiatric disorders. The analyses were repeated for the 2 largest groups of persons with specific anxiety disorder diagnoses, generalized anxiety disorder and agoraphobia. When we found that the relationship between TST and depressive and anxiety disorders was best described by a quadratic model, we repeated the analyses with categories of TST (< 5, 5 to < 6, 6 to < 7, 7 to < 8, 8 to < 9, and ≥ 9 hours) to illustrate the results. These last analyses were repeated 3 times: first, after exclusion of persons with excessive alcohol consumption; second, after exclusion of persons with probable sleep apnea; and third, in the participants who did not use psychoactive medication (n = 3,862).

As the main analyses showed that both long and short sleep durations were associated with depression, we performed additional analyses to examine whether the 2 tails of the distribution reflected different characteristics. In particular, we examined whether the group of depressive persons with short TST (< 7 hours, n = 99) differed from the group of depressive persons with long TST (≥ 8 hours, n = 48) with respect to comorbidity with functional disability and the number of depressive symptoms. Physical symptoms may cause or aggravate poor sleep, and long—or short—sleep may reflect a more severe subtype of depression. All of the analyses were adjusted for age and gender. All analyses were performed with SPSS version 11.0 (SPSS Inc, Chicago, Illinois).

RESULTS

Table 1 presents the characteristics of the study population. Of the 5,019 participants in our study, 56.7% were female, and the mean age was 72.4 years (SD = 7.6; range, 58–100). Table 2 shows the mean sleep parameters and the prevalence of depressive disorders and anxiety disorders in the study population. *DSM-IV-TR* criteria for a depressive disorder were met by 179 participants (3.6% of the total study population); 407 (8.1%) had one or more anxiety disorders. Participants reported a mean of 6.88 (SD = 1.27) hours of sleep per night.

Table 3 shows the age- and gender-adjusted estimated means of TST, SOL, TIB, and global PSQI score for groups of participants with depressive disorders, anxiety disorders, or both. Total sleep time in persons with a depressive disorder only, or an anxiety disorder only, did not differ from TST of persons in the reference category. However, participants with both disorders reported a 1.07-hour (95% CI = –1.37 to –0.76) shorter TST than persons without these disorders. Sleep onset latency was 8.9 minutes (95% CI = 3.7 to 14.1)

© Copyright 2009 Physicians Postgraduate Press, Inc. © Copyright 2009 Physicians Postgraduate Press, Inc.

Table 3. Sleep Parameters in Depressive and Anxiety Disorders (N = 5,019)[a]

Sleep Parameter	Reference Category[b] (n = 4,499), Estimated Mean	Depressive Disorder, No Anxiety Disorder (n = 113)			Anxiety Disorder, No Depressive Disorder (n = 341)			Both Depressive and Anxiety Disorders (n = 66)		
		Estimated Mean	Difference With Reference (95% CI)	*P* Value of Difference	Estimated Mean	Difference With Reference (95% CI)	*P* Value of Difference	Estimated Mean	Difference With Reference (95% CI)	*P* Value of Difference
Total sleep time, h	6.91	6.90	−0.01 (−0.25 to 0.22)	.91	6.80	−0.10 (−0.24 to 0.04)	.14	5.84	−1.07 (−1.37 to −0.76)	< .001
Sleep onset latency, min	20.8	29.7	8.9 (3.7 to 14.1)	.001	26.4	5.6 (2.5 to 8.7)	< .001	36.0	15.2 (8.4 to 22.0)	< .001
Time in bed, h	7.73	8.06	0.33 (0.13 to 0.54)	.002	7.82	0.09 (−0.04 to 0.21)	.16	7.53	−0.20 (−0.47 to 0.07)	.14
PSQI score	3.7	6.2	2.5 (1.9 to 3.1)	< .001	4.8	1.1 (0.8 to 1.5)	< .001	8.6	4.9 (4.1 to 5.8)	< .001

[a]Statistical test is analysis of covariance. All analyses are adjusted for age and gender.
[b]No depressive disorder, no anxiety disorder.
Abbreviation: PSQI = Pittsburgh Sleep Quality Index.

longer in depressed participants than in the reference category, 5.6 minutes (95% CI = 2.5 to 8.7) longer in persons with an anxiety disorder, and 15.2 minutes (95% CI = 8.4 to 22.0) longer in participants with both disorders, which confirms our hypothesis. Time in bed was significantly longer in participants with only a depressive disorder than in any of the other groups (Table 3).

Table 4 shows that the relationship of TST with depressive disorders was adequately described by a quadratic U-shaped model (OR of quadratic term = 1.10; 95% CI = 1.05 to 1.15, $P < .001$), as well as the relationship of TST with anxiety disorders (OR of quadratic term = 1.06; 95% CI = 1.02 to 1.20, $P = .002$). Linear models were also significant for depressive disorders as well as anxiety disorders, both with ORs < 1.00, indicating that the associations of short sleep with both disorders were stronger than were the associations of long sleep.

The analyses were repeated for the 2 largest groups of persons with specific anxiety disorder diagnoses, generalized anxiety disorder (n = 111) and agoraphobia without history of panic disorder (n = 195). This repeated analysis showed that TST also had a clear quadratic relationship with generalized anxiety disorder (OR of quadratic term = 1.10; 95% CI = 1.04 to 1.17, $P = .001$). The relationship of TST with agoraphobia, however, was best described by a linear model (OR = 0.89, 95% CI = 0.80 to 1.00, $P = .04$); a quadratic model was not significant. This indicates that short sleepers were more likely to have this disorder than long sleepers.

To illustrate the quadratic relationships, Figure 2 presents the associations of categories of TST with depressive disorders, and Figure 3 presents the associations of TST with anxiety disorders. Figure 2 shows that persons with a TST of < 6 hours and persons with a TST of ≥ 9 hours were more likely to have a depressive disorder than were persons in the reference category of 7 to < 8 hours. The ORs for depression of persons with a TST of < 5 hours, 5 to < 6 hours, and ≥ 9 hours were all significant at the $P < .001$ level, whereas only persons in the lowest category of TST, < 5 hours, had a significantly higher risk of having an anxiety disorder ($P < .001$) in comparison with the reference category. After exclusion of persons with excessive alcohol use (n = 531), the odds ratios were slightly attenuated, eg, the OR for depression of the TST < 5-hour category changed from 4.60 (95% CI = 2.68 to 7.90) to 4.20 (95% CI = 2.41 to 7.33), but all of the associations remained highly significant. Exclusion of persons with probable sleep apnea (n = 403) slightly increased the odds ratios; eg, the OR for depression of the TST < 5-hour category was now 5.01 (95% CI = 2.88 to 8.70), but the U-shaped pattern did not change. However, exclusion of persons who used psychoactive medication substantially changed the results. Figures 2 and 3 also present the results of the same analyses in a subgroup of participants who used no psychoactive medication. The ORs of depression in the lowest TST categories, as well as the OR of anxiety disorders in the TST < 5-hour category, were substantially higher than the

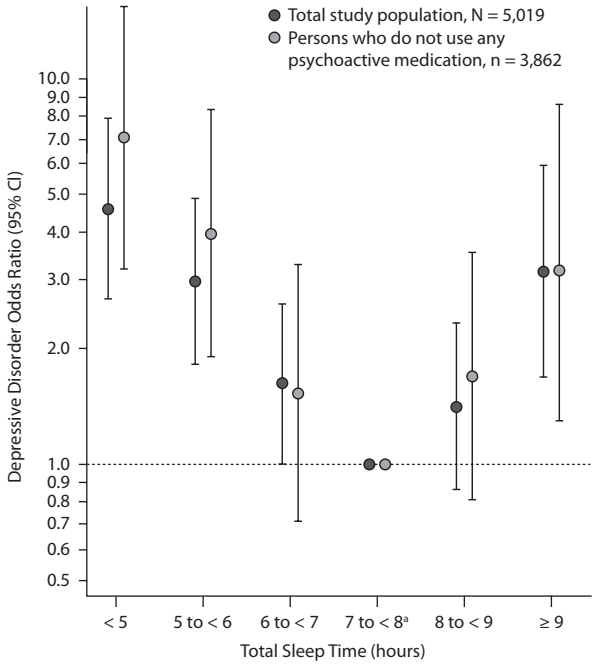
COPYRIGHT 2009 PHYSICIANS POSTGRADUATE PRESS, INC. © COPYRIGHT 2009 PHYSICIANS POSTGRADUATE PRESS, INC.

Table 4. Association of Total Sleep Time With *DSM-IV-TR* Depressive and Anxiety Disorders (N = 5,019)[a]

Model	*DSM-IV-TR* Depressive Disorders		*DSM-IV-TR* Anxiety Disorders	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Linear model				
Total sleep time, h	0.80 (0.71 to 0.89)	< .001	0.86 (0.79 to 0.93)	< .001
Quadratic model				
Total sleep time, h	0.24 (0.13 to 0.42)	< .001	0.40 (0.25 to 0.65)	< .001
Total sleep time^2, h^2	1.10 (1.05 to 1.15)	< .001	1.06 (1.02 to 1.20)	.002

[a]Statistical test is logistic regression. All analyses are adjusted for age and gender.

Figure 2. Association of Categories of Total Sleep Time With *DSM-IV-TR* Depressive Disorders

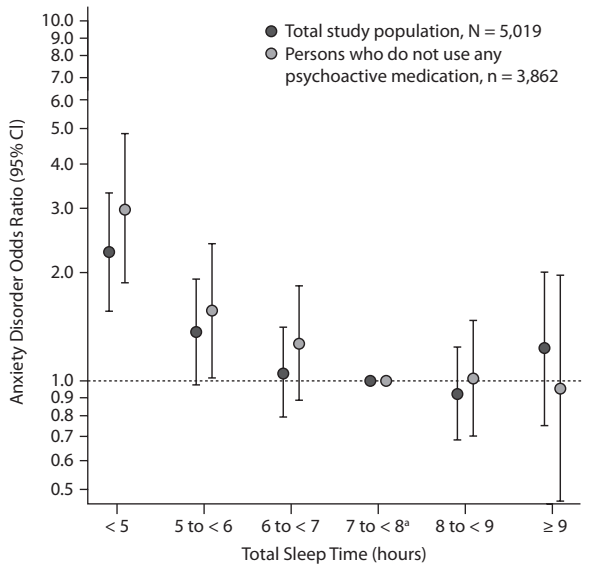


[a]Reference category.

ORs in the total study population. This prompted us to perform an additional stratified analysis (results not shown). In the group of persons who used psychoactive medication, the ORs for the lowest TST categories fell outside the CIs of the ORs in the group without psychoactive medication: eg, the OR for depression in the lowest TST category of < 5 hours was 2.49 (95% CI = 1.12 to 5.57), whereas, in persons without medication, it was 7.01 (95% CI = 3.21 to 15.3).

To conclude, we compared comorbidity with functional disability, as a measure of general medical condition, and we compared CES-D scores (number of depressive symptoms) between depressive persons with short TST (< 7 hours, n = 99) and depressive persons with long TST (≥ 8 hours, n = 48). When analyses were adjusted for age and gender, there were no significant differences between these groups in functional disability (data not shown). However, depressed persons with short sleep had higher CES-D scores than did depressed persons with long sleep (28.1 vs 24.6; *P* = .02, analysis of covariance).

Figure 3. Association of Categories of Total Sleep Time With *DSM-IV-TR* Anxiety Disorders



[a]Reference category.

DISCUSSION

In this cross-sectional study of 5,019 community-dwelling elderly subjects, we found that the mean TST in elderly persons with either a depressive disorder or an anxiety disorder did not differ from the mean TST of those without these disorders. Rather, both short and long sleepers were more likely to have a depression or anxiety disorder. These associations were stronger in participants who did not use psychoactive medication. When TIB, instead of TST, was analyzed in relation to depressive disorders, we found that persons with a depressive disorder did spend more time in bed than nondepressed persons. Finally, participants with a depressive disorder and a comorbid anxiety disorder reported a substantially shorter TST than other elderly persons.

Our study has several strengths. First, it is a large population-based study. In a community sample, one may encounter milder and untreated forms of psychiatric disorders that are not present in clinical samples. Moreover, it has been shown that persons with psychiatric disorders who do not seek help are different from patient populations, also with respect to sleep disturbance in depression.[35] Second, *DSM-IV-TR* diagnoses of depressive disorders were

© Copyright 2009 Physicians Postgraduate Press, Inc. © Copyright 2009 Physicians Postgraduate Press, Inc.

carefully ascertained by experienced clinicians. Epidemiologic research on this subject is often based on less precise measures of depressive disorders, which can result in misclassification. This methodological difference may explain the low prevalence of depression in our study in comparison with other epidemiologic studies in elderly persons.[36]

However, our study also has some limitations. First, the CIDI, which we used to assess anxiety disorders, is a lay-administered diagnostic interview that is not equivalent to an experienced clinician's assessment. Second, our assessment of anxiety disorders did not include acute stress disorder, posttraumatic stress disorder, and obsessive-compulsive disorder. This implies that some persons in the "no anxiety disorder" categories may in fact have had one of these anxiety disorders. Third, we combined different categories of depressive disorders and also of anxiety disorders in order to obtain sufficient statistical power for our analyses. However, 2 of the anxiety disorder categories could be analyzed separately. There was some evidence that different categories of anxiety disorders have different relationships with sleep. Fourth, the cross-sectional design of our study precluded the inference of temporal relationships. Fifth, we used self-report measures of sleep. Although we used a validated questionnaire, self-report measures can be biased, in particular in depressed persons.[37] Finally, our study population consisted mainly of elderly white Dutch persons, which, strictly speaking, limits the generalizability of the study. However, we do not have reasons to expect that the mechanisms underlying the relationships between sleep and psychiatric disorders are substantially different in other ethnic groups.

In this study, we assessed TST, TIB, and SOL by questionnaire; these parameters have rarely been studied in relation to psychiatric disorders in large population samples. In some studies, TST and TIB are used interchangeably,[38] which makes it unclear what exactly is meant by "long or short sleep." Only when both TST and TIB are taken into account, short sleep due to insomnia or sleep disturbance can be distinguished from short sleep with high sleep efficiency. The latter may be due to voluntary sleep restriction or less need of sleep.

Our analyses of TST confirmed our hypothesis of an association of both short and long TST with depression. This is in accordance with the observation that both insomnia and hypersomnia can be symptoms of depressive disorders.[23] Taylor et al[14] noted that self-reported insomnia was strongly associated with both depressive and anxiety symptoms in a community-based study of 772 persons. However, they did not find any association between TST or SOL and depression or anxiety. This may have resulted from their assessment of depression and anxiety with self-report questionnaires, which is a less precise method than psychiatric interviews. Also, they did not present models with quadratic terms. Chang et al[13] studied insomnia as a risk factor for depression in young men. They found that insomnia and, to a lesser extent, sleeping ≤ 7 hours per night increased the risk of subsequent depression. Studies such as these, which focus on sleep disturbance as a precursor of depressive disorders, rarely discuss long sleep or long TIB. A cross-sectional association between long sleep and depression has been previously reported.[2] The U-shaped curve has also been described previously in 3 Japanese studies[1,15,39]: both long and short sleep were related to depressive symptoms, as measured by CES-D, in Japanese adults[1,15] and to subjective well-being in Japanese elderly.[39] We found the U-shaped curve with psychiatric disorders that were diagnosed according to *DSM-IV-TR*. We also found that depressed persons with short TST had higher CES-D scores than did depressed persons with long TST, which may suggest that short sleepers have more severe depressions.

The results of our analyses with TIB did not follow the same pattern as the results of TST. We found that depressed individuals, on average, reported longer TIB than did nondepressed persons, unless they also had a comorbid anxiety disorder. Spending much time in bed may be a result of symptoms of depression, such as fatigue, loss of energy, loss of interest or pleasure in activities, or indecisiveness.[23] The complex interrelatedness of depression, TST, and TIB is probably best described by 2 separate mechanisms. On the one hand, poor sleep or too little sleep may be both a precursor and a consequence of depression.[4–6,8,12,13] On the other hand, long sleep is closely related to long TIB and is more likely to be a symptom or consequence of depression.

Whether a depression is characterized by insomnia or by long sleep and spending much time in bed may be a difference between individuals, or sleep patterns may change in the course of a depressive disorder. In an elderly population, circadian rhythms are less entrained by work and other duties than in younger persons. Therefore, the relationship between long sleep (and long TIB) and depression may be particularly apparent in elderly persons. However, hypersomnia as a symptom of depression is likely to occur in younger persons as well.

To the best of our knowledge, no previous studies have investigated the association between sleep parameters and anxiety disorders in a population-based setting. We observed that the association between TST and anxiety disorders could also be described by a quadratic model. Our hypothesis concerning a relationship between short sleep and anxiety was confirmed, but, apparently, long sleep duration is, to some extent, associated with anxiety disorders too, although the quadratic relationship is less marked than with depression. Sleep onset latency and subjective sleep quality were also significantly impaired in persons with anxiety disorders. This is in accordance with our hypotheses, as anxiety disorders manifest with heightened arousal, which is also implicated when sleep initiation or maintenance are disturbed.[21] Interestingly, TST had a clear quadratic relationship with generalized anxiety disorder, whereas the relationship of TST with agoraphobia was best described

© Copyright 2009 Physicians Postgraduate Press, Inc.

© Copyright 2009 Physicians Postgraduate Press, Inc.

by a linear model. This suggests that different mechanisms are involved in sleep disturbance in these specific disorders. Ford and Kamerow[4] also reported a higher risk of depression as well as anxiety disorders in persons with insomnia, as well as in persons with hypersomnia. They noted that the relationship between anxiety disorders and sleep disturbances followed a pattern similar to that between depression and sleep disturbances, although the ORs were lower. However, apart from self-reported sleep complaints, they did not investigate other sleep parameters.

Comorbidity of depressive disorders and anxiety disorders is common.[4,22,40] In this study, TST was substantially shorter in persons with both a depressive disorder and an anxiety disorder, although the mean TIB of these persons did not differ significantly from the mean TIB in the reference group. Comorbidity of depression and anxiety disorders was also related to substantially worse self-reported sleep quality in terms of SOL and global PSQI score. These results suggest that persons with both disorders suffer from major sleep disturbance. Roth et al[41] investigated the relationship between comorbidity of psychiatric disorders and the occurrence of sleep problems. They reported that respondents meeting criteria for 3 or more 12-month *DSM-IV-TR* disorders had much higher odds of sleep problems than did respondents with 1 or 2 *DSM-IV-TR* disorders.[41]

Thase[42] demonstrated that antidepressants exert both beneficial and, at times, detrimental effects on subjective and objective measures of sleep. Because of the large number of participants in our study, we were able to study the association of TST with depression and anxiety disorders in participants who did not use antidepressants, anxiolytics, sedatives, or hypnotics. In this subgroup, the associations of short TST with depression and anxiety disorders were stronger than in the total study population; in the group of persons who used psychoactive medication, the associations were markedly weaker. This suggests that medication use increases (perceived) sleep duration in depressed persons. Another possible explanation for this finding is that the use of psychoactive medication lowers the risk of depression and anxiety disorders in short sleepers. Contrary to what might be expected, our results do not indicate that severity of sleep-related symptoms increases the likelihood of medication use. This confounding by indication would have led to weaker associations between short TST and psychiatric disorders in an unmedicated subgroup.

In summary, sleep parameters and psychiatric disorders are intertwined in complex ways. We found that both long and short TST are associated with depressive disorders in an elderly population, and, similarly, the association between TST and anxiety disorders can also be described best by a quadratic model. The use of psychoactive medication appears to attenuate these relationships. For a better understanding of the etiology of depression and anxiety disorders, it is important to know that different phenotypes of these disorders with regard to sleep exist in the general population. Clinicians should be aware that, on the one hand, depressed persons with long TST have less depressive symptoms than persons who report habitual sleep durations of < 6 hours, which thus may indicate more severe depression. Also, TST is substantially shorter in persons who have depressive disorder and a comorbid anxiety disorder. On the other hand, depression can also be accompanied by longer-than-average sleep durations, and particularly by a long TIB. Therefore, clinicians should also pay attention to oversleeping as a possible sign of a psychiatric disorder. Restricting TIB may alleviate depressive symptoms in these persons.[43] Future research in the general population with objective measures of sleep parameters may contribute to a better understanding of the relationships of sleep parameters with psychiatric disorders.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this article.
Author affiliations: Departments of Epidemiology (Drs van den Berg, Luijendijk, Hofman, and Tiemeier), Psychiatry (Dr Tulen), and Child and Adolescent Psychiatry (Dr Tiemeier), Erasmus Medical Center, Rotterdam; Department of Public Health and Primary Care, Leiden University Medical Center, Leiden (Drs van den Berg and Knuistingh Neven); and Department of Geriatric Psychiatry, Parnassia BAVO Group, Institution for Mental Health Care, Rotterdam (Dr Luijendijk), The Netherlands.
Financial disclosure: **Drs van den Berg**, **Luijendijk**, **Tulen**, **Hofman**, **Knuistingh Neven**, and **Tiemeier** have no personal affiliations or financial relationships with any commercial interest to disclose relative to the article.
Funding/support: The Rotterdam Study is supported by the Erasmus Medical Center and Erasmus University Rotterdam; the Netherlands Organization for Scientific Research (NWO); the Netherlands Organization for Health Research and Development (ZonMw); the Research Institute for Diseases in the Elderly (RIDE); the Ministry of Education, Culture and Science; the Ministry of Health, Welfare and Sports; the European Commission (DG XII); and the Municipality of Rotterdam. Additional funding for the sleep research project was provided by ZonMw grant 4200.0019.

REFERENCES

1. Tamakoshi A, Ohno Y. Self-reported sleep duration as a predictor of all-cause mortality: results from the JACC study, Japan. *Sleep.* 2004;27(1):51–54.
2. Patel SR, Malhotra A, Gottlieb DJ, et al. Correlates of long sleep duration. *Sleep.* 2006;29(7):881–889.
3. Ancoli-Israel S, Ayalon L. Diagnosis and treatment of sleep disorders in older adults. *Am J Geriatr Psychiatry.* 2006;14(2):95–103.
4. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? *JAMA.* 1989;262(11):1479–1484.
5. Tsuno N, Besset A, Ritchie K. Sleep and depression. *J Clin Psychiatry.* 2005;66(10):1254–1269.
6. Roberts RE, Shema SJ, Kaplan GA, et al. Sleep Complaints and Depression in an Aging Cohort: A Prospective Perspective. *Am J Psychiatry.* 2000;157(1):81–88.
7. Riemann D, Berger M, Voderholzer U. Sleep and depression - results from psychobiological studies: an overview. *Biol Psychol.* 2001;57(1–3):67–103.
8. Fava M. Daytime sleepiness and insomnia as correlates of depression. *J Clin Psychiatry.* 2004;65(suppl 16):27–32.
9. Grandner MA, Drummond SPA. Who are the long sleepers? Towards an understanding of the mortality relationship. *Sleep Med Rev.* 2007; 11(5):341–360.

© Copyright 2009 Physicians Postgraduate Press, Inc. © Copyright 2009 Physicians Postgraduate Press, Inc.

10. Ayas NT, White DP, Manson JE, et al. A Prospective Study of Sleep Duration and Coronary Heart Disease in Women. *Arch Intern Med.* 2003;163(2):205–209.
11. Buysse DJ. Insomnia, depression and aging. Assessing sleep and mood interactions in older adults. *Geriatrics.* 2004;59(2):47–51.
12. Riemann D, Voderholzer U. Primary insomnia: a risk factor to develop depression? *J Affect Disord.* 2003;76(1–3):255–259.
13. Chang PP, Ford DE, Mead LA, et al. Insomnia in young men and subsequent depression. The Johns Hopkins Precursors Study. *Am J Epidemiol.* 1997;146(2):105–114.
14. Taylor DJ, Lichstein KL, Durrence HH, et al. Epidemiology of insomnia, depression, and anxiety. *Sleep.* 2005;28(11):1457–1464.
15. Kaneita Y, Ohida T, Uchiyama M, et al. The relationship between depression and sleep disturbances: a Japanese nationwide general population survey. *J Clin Psychiatry.* 2006;67(2):196–203.
16. Belanger L, Morin CM, Langlois F, et al. Insomnia and generalized anxiety disorder: Effects of cognitive behavior therapy for GAD on insomnia symptoms. *J Anxiety Disord.* 2004;18(4):561–571.
17. Monti JM, Monti D. Sleep disturbance in generalized anxiety disorder and its treatment. *Sleep Med Rev.* 2000;4(3):263–276.
18. Saletu-Zyhlarz G, Saletu B, Anderer P, et al. Nonorganic insomnia in generalized anxiety disorder. 1. Controlled studies on sleep, awakening and daytime vigilance utilizing polysomnography and EEG mapping. *Neuropsychobiology.* 1997;36(3):117–129.
19. Lepola U, Koponen H, Leinonen E. Sleep in panic disorders. *J Psychosom Res.* 1994;38(suppl 1):105–111.
20. Beekman AT, Bremmer MA, Deeg DJ, et al. Anxiety disorders in later life: a report from the Longitudinal Aging Study Amsterdam. *Int J Geriatr Psychiatry.* 1998;13(10):717–726.
21. Stein MB, Mellman TA. *Anxiety Disorders. Principles and Practice of Sleep Medicine*. 4th ed. Philadelphia, PA: Elsevier Saunders; 2005:1297–1310.
22. De Graaf R, Bijl RV, Smit F, et al. Risk factors for 12-month comorbidity of mood, anxiety, and substance use disorders: findings from the Netherlands Mental Health Survey and Incidence Study. *Am J Psychiatry.* 2002;159(4):620–629.
23. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision. Washington, DC: American Psychiatric Association; 2000.
24. Hofman A, Breteler MM, van Duijn CM, et al. The Rotterdam Study: objectives and design update. *Eur J Epidemiol.* 2007;22(11):819–829.
25. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12(3):189–198.
26. Buysse DJ, Reynolds CF 3rd, Monk TH, et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.* 1989;28(2):193–213.
27. Beekman ATF, Deeg DJH, van Limbeek J, et al. Criterion validity of the Center for Epidemiologic Studies Depression scale (CES-D): results from a community-based sample of older subjects in the Netherlands. *Psychol Med.* 1997;27(1):231–235.
28. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas.* 1977;1(3):385–401.
29. World Health Organization Division of Mental Health. *SCAN Schedules for Clinical Assessment in Neuropsychiatry.* Version 2.1. Geneva, Switzerland: World Health Organization; 1997.
30. World Health Organization. *Composite International Diagnostic Interview (CIDI)*, version 2.1, January 1997. Geneva, Switzerland: World Health Organization; 1998.
31. Wittchen H-U, Lachner G, Wunderlich U, et al. Test-retest reliability of the computerized *DSM-IV* version of the Munich-Composite International Diagnostic Interview (M-CIDI). *Soc Psychiatry Psychiatr Epidemiol.* 1998;33(11):568–578.
32. Fries JF, Spitz PW, Young DY. The dimensions of health outcomes: the health assessment questionnaire, disability and pain scales. *J Rheumatol.* 1982;9(5):789–793.
33. Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: dimensions and practical applications. *Health Qual Life Outcomes.* 2003;1:20.
34. Fogelholm M, Kronholm E, Kukkonen-Harjula K, et al. Sleep-related disturbances and physical inactivity are independently associated with obesity in adults. *Int J Obes (Lond).* 2007;31(11):1713–1721.
35. Vitiello MV, Prinz PN, Avery DH, et al. Sleep is undisturbed in elderly, depressed individuals who have not sought health care. *Biol Psychiatry.* 1990;27(4):431–440.
36. Beekman AT, Deeg DJ, van Tilburg T, et al. Major and minor depression in later life: a study of prevalence and risk factors. *J Affect Disord.* 1995;36(1–2):65–75.
37. van den Berg JF, Van Rooij FJA, Vos H, et al. Disagreement between subjective and actigraphic measures of sleep duration in a population-based study of elderly persons. *J Sleep Res.* 2008;17(3):295–302.
38. Jean-Louis G, Kripke DF, Ancoli-Israel S. Sleep and quality of well-being. *Sleep.* 2000;23(8):1115–1121.
39. Yokoyama E, Saito Y, Kaneita Y, et al. Association between subjective well-being and sleep among the elderly in Japan. *Sleep Med.* 2008;9(2):157–164.
40. Kessler RC, Chiu WT, Demler O, et al. Prevalence, Severity, and Comorbidity of 12-Month *DSM-IV* Disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry.* 2005;62(6):617–627.
41. Roth T, Jaeger S, Jin R, et al. Sleep problems, comorbid mental disorders, and role functioning in the national comorbidity survey replication. *Biol Psychiatry.* 2006;60(12):1364–1371.
42. Thase ME. Depression, sleep, and antidepressants. *J Clin Psychiatry.* 1998;59(suppl 4):55–65.
43. Giedke H, Schwärzler F. Therapeutic use of sleep deprivation in depression. *Sleep Med Rev.* 2002;6(5):361–377.

For the CME Posttest for this article, see pages 1197–1198.

COPYRIGHT 2009 PHYSICIANS POSTGRADUATE PRESS, INC. © COPYRIGHT 2009 PHYSICIANS POSTGRADUATE PRESS, INC.