Subjective and Objective Sleep Disturbance and Longitudinal Risk of Depression in a Cohort of Older Women

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Objective: To investigate the longitudinal relationship between subjective and objective sleep disturbance and depressive symptoms.
Design: Longitudinal.
Setting: Three US clinical centers.
Participants: Nine hundred fifty-two community-dwelling older women (70 y or older).
Measurements: At baseline, subjective sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) and objective sleep measures were assessed with wrist actigraphy. Depressive symptoms were assessed with the Geriatric Depression Scale (GDS) at baseline and approximately 5 y later. The analysis was restricted to women with few (GDS 0-2) depressive symptoms at baseline.
Results: There was an independent association between greater PSQI score (per standard deviation increase, indicating worse subjective sleep quality) at baseline and greater odds of worsening depressive symptoms (≥ 2-point increase in GDS) (Multivariate Odds Ratio [MOR] 1.19, confidence interval [CI] 1.01-1.40, P = 0.036). Higher scores specifically on the sleep quality (MOR 1.41, CI 1.13-1.77, P < 0.003) and sleep latency (MOR 1.21, CI 1.03-1.41, P = 0.018) PSQI subscales were also associated with greater odds for worsening depressive symptoms. Objective assessments revealed an association between baseline prolonged wake after sleep onset (WASO ≥ 60 min) and worsening depressive symptoms at follow-up (MOR 1.36, CI 1.01-1.84, P = 0.046). There were no associations between other objectively assessed sleep measures and worsening depressive symptoms.
Conclusions: In older women with few or no depressive symptoms at baseline, those with more subjectively reported sleep disturbance and more objectively assessed fragmentation of sleep at baseline had greater odds of worsening depressive symptoms 5 y later. Future studies investigating this relationship in more detail are indicated.
Keywords: actigraphy, age, depression, elderly, sleep
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INTRODUCTION

Depressive syndromes are common in older adults. For example, in primary care settings, the prevalence of major depressive disorder in this age group is 3-10%,[1-4] and subthreshold depressive syndromes (including dysthymia, minor depression, and subsyndromal depression) are estimated to be more common (9-24%).[2,5–8] Further, depressive syndromes may have a greater prevalence in hospital and long-term care settings.[9] Depressive syndromes in older adults are associated with adverse outcomes including functional impairment,[10,11] medical illnesses,[12] disability,[13,14] increased mortality,[15] and increased health services utilization.[16] Longitudinal studies have shown that subjective sleep disturbance is a major risk factor for future development of both first-onset and recurrent depressive episodes in both younger and older adults.[17–20]

Also, persistent subjective sleep disturbance has been shown to increase risk of depression longitudinally sixfold to 34-fold.[19,21] However, there is a paucity of information regarding the longitudinal relationship between objectively measured sleep disturbances and risk for depression. The longitudinal relationship between sleep disturbances and subthreshold levels of depressive symptoms also remains unexplored.

A cross-sectional study in a group of community-dwelling older men found a strong, graded association between subjective sleep disturbance and increased level of depressive symptoms as well as a more modest association between objectively measured (by actigraphy) increased sleep latency and increased level of depressive symptoms.[22] A similar cross-sectional analysis in community-dwelling older women also demonstrated a strong, graded association between more subjective sleep disturbance and greater levels of depressive symptoms. In the older women, assessment of sleep by actigraphy revealed associations between objective measures of sleep fragmentation and greater levels of depressive symptoms.[23]
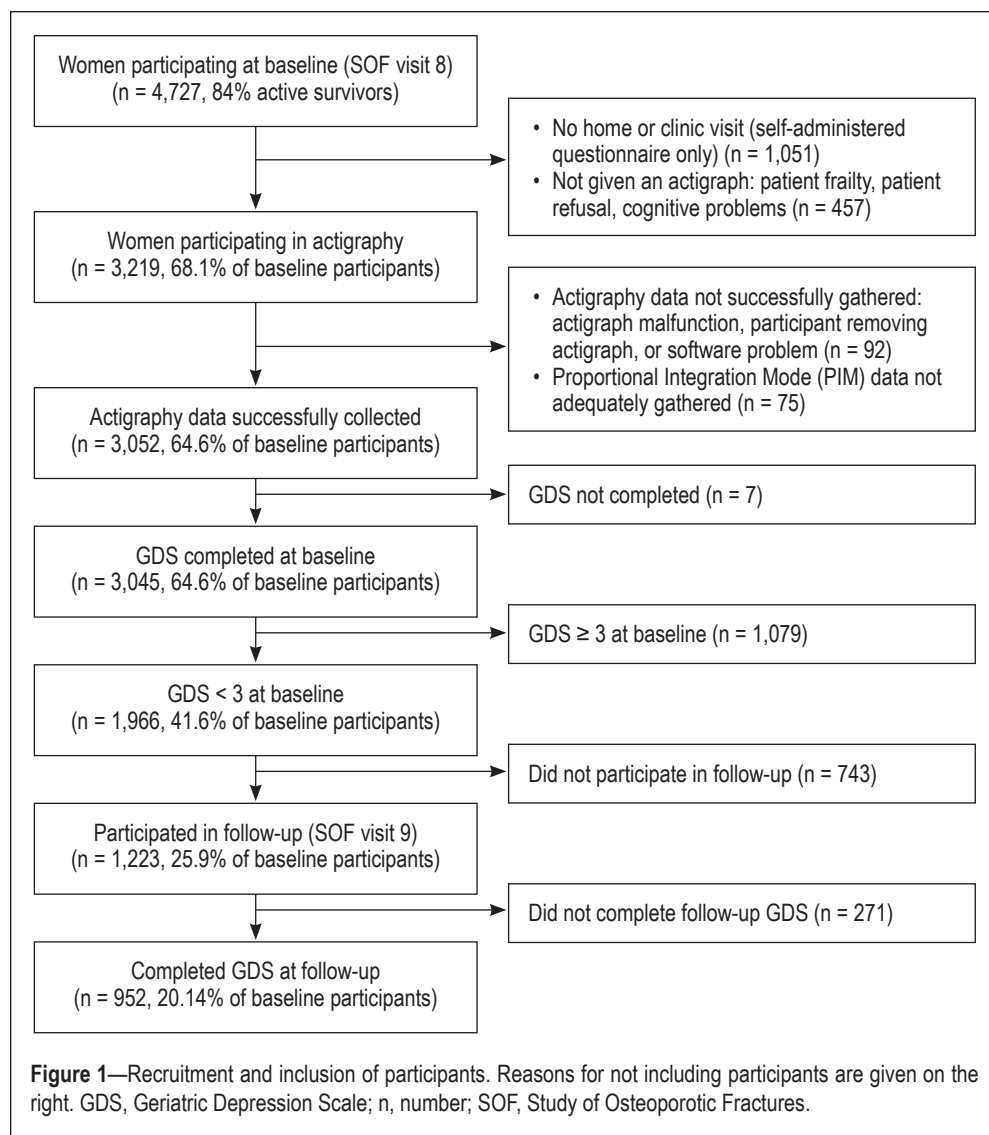
The goal of the current study was to explore the longitudinal relationship between baseline subjectively and objectively assessed sleep measures and future depressive symptoms in a group of older women who reported few or no depressive symptoms at baseline. We hypothesized that nondepressed older women with subjectively and objectively measured disturbances in sleep at baseline would be at greater risk for endorsing more depressive symptoms at follow-up.

Figure 1—Recruitment and inclusion of participants. Reasons for not including participants are given on the right. GDS, Geriatric Depression Scale; n, number; SOF, Study of Osteoporotic Fractures.

METHODS

Participants

Participants were women enrolled in the Study of Osteoporotic Fractures (SOF), an ongoing, multicenter, prospective cohort study of primarily Caucasian, community-dwelling women age 65 y and older from four geographic areas (Portland, OR; Minneapolis, MN; Pittsburgh, PA/Monongahela Valley, PA; Baltimore, MD). Women gave informed consent prior to enrollment in the study. Between September 1986 and October 1988, the 9,704 participants making up the original cohort were recruited via community listings and mailed announcements. Between February 1997 and February 1998, 662 African American women were also recruited. Women were excluded from participation if they required assistance with ambulation or had undergone bilateral hip replacement. Details regarding the study have been published.[24] The current analyses focused on women participating in SOF visits 8 and 9 (approximately 15 and 20 y after the original assessment). There were 4,727 participants at visit 8, representing 84% of active survivors. Of these women, 3,219 participated in objective assessment of sleep by actigraphy at visit 8, and objective sleep data was

successfully collected for 3,127 women. Reasons for unsuccessful collection (n = 92) included having an actigraph malfunction, software initialization problem, removing the actigraph and not replacing it, and data not being collected or saved successfully at the clinic site. Three thousand forty-five women returned completed Geriatric Depression Scale (GDS) questionnaires at visit 8 and 1,966 of them reported few depressive symptoms (GDS 0-2). Of these women, 952 women participated in a clinic assessment at follow-up and completed GDS questionnaires at that time. The Baltimore site did not participate in visit 9, preventing 359 women from following-up. The current analyses were performed on this subset of 952 women (Figure 1).

Subjective Sleep Measures

Baseline subjective sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), a validated19-item self-report questionnaire. PSQI items may be grouped into seven subcomponent scores: sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, sleep medication use, and daytime dysfunction. Each subcomponent score ranges from 0-3, with higher scores reflecting more symptoms. These subcomponent scores can be summed to create a total score, with higher scores reflecting worse sleep. PSQI total and subcomponent scores were expressed as continuous variables. PSQI total score was also expressed as a dichotomous variable: PSQI > 5 versus. PSQI ≤ 5. A total score > 5 has a sensitivity of 89.6% and specificity of 86.5% for distinguishing good sleepers from poor sleepers.[25]

Objective Sleep Measures

Baseline objective sleep parameters were measured using wrist actigraphy, a previously validated[26–28] noninvasive tool that provides information about sleep and wake patterns via an accelerometer that detects wrist movement. Actigraphs (SleepWatch-O, Ambulatory Monitoring, Inc, Ardsley, NY) were worn on participants' nondominant wrist for at least three consecutive 24-h periods (mean 4.1 ± 0.7 nights). Movements were recorded and summarized in 1-min epochs. The data were collected using the proportional integration mode[27] and analyzed using ActionW-2 software (Ambulatory Monitoring, Inc). The University of California San Diego algorithm was used to distinguish sleep from wake.[29,30] Participants also completed sleep diaries for the time period they wore the

actigraph, including information about times they got into and out of bed and times their actigraph was removed. This information was used in editing the actigraphy data to set intervals for when the participant was in bed trying to sleep and to delete time when the actigraph was removed. In the SOF study, interscorer reliability for editing the actigraphy data files has been previously found to be high (total sleep time (TST)/intraclass coefficient = 0.95), and TST estimated via actigraphy has been shown to have good concordance with TST assessed by polysomnography (PSG).[26,27]

The following variables were used in the analyses: TST, sleep efficiency (SE, percent of time asleep while in bed), sleep onset latency (SOL, min between bed time and the first block of inactivity after bed time), WASO (min awake between sleep onset and wake time), and number of long wake episodes (number of wake episodes between sleep onset and wake time exceeding 5 min). Data for each variable were averaged over the recorded time. Objective sleep variables were expressed as dichotomous variables. Specific categories included SE < 85% versus SE ≥ 85%, SOL ≥ 60 min versus SOL < 60 min, WASO ≥ 60 min versus WASO < 60 min, number of long wake episodes ≥ 8 versus number of long wake episodes < 8. TST was expressed as a three-level variable including < 5 h (short sleep duration), 5-8 h (normal sleep duration), and > 8 h (prolonged sleep duration). These cutoff points were chosen to be consistent with our previous cross-sectional analysis of associations between sleep disturbances and depressive symptoms in this cohort.[23]

Depressive Symptoms

Depressive symptoms were assessed using the GDS, a 15-item validated self-report questionnaire commonly used for assessment of depressive symptoms in older adults,[31] at baseline and follow-up. For the primary analyses, women were categorized into three groups (0-2 [no or few depressive symptoms], 3-5 [some depressive symptoms], ≥ 6 [many depressive symptoms]) according to depressive symptoms endorsed at follow-up. For simplicity and to remain consistent with prior publications using this strategy,[22] the ≥ 6 GDS group was referred to as "depressed." A standard cutoff of ≥ 6 on the GDS has been shown to have a sensitivity of 91% and specificity of 65% for diagnosis of a major depressive episode compared with the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.[32] For the secondary analyses, change in GDS score between baseline and follow-up was calculated for each participant. Women with a ≥ 2-point increase in GDS score were considered to have "worsening depressive symptoms." This cutpoint was chosen, based on the distribution of change in GDS scores in our sample, because it distinguished women with the greatest increase in GDS score (highest quartile) between baseline and follow-up.

Covariables

Demographic information (birth date, ethnicity, years of education) was recorded at the original assessment. At each visit, participants completed questionnaires regarding health status, smoking, alcohol consumption, caffeine intake, exercise habits, and medical history. Women rated their health status as excellent, good, fair, poor, or very poor and were asked whether they walked for exercise. They were also asked whether they

had specific medical diagnoses. Reported medical conditions included in these analyses were stroke, diabetes, Parkinson disease, chronic obstructive pulmonary disease, congestive heart failure, myocardial infarction, thyroid disease, hypertension, other neurological condition, other cardiac condition, osteoarthritis, rheumatoid arthritis, osteoporosis, and cancer. Self-reported average daily intake of caffeinated beverages (coffee, soda, and tea) was used to estimate the average daily caffeine intake, assuming 95 mg for a cup of coffee, 55 mg for a cup of tea, and 45 mg for a can of soda.[33] A clinic interview included an assessment of impairments in instrumental activities of daily living (IADLs) in which the patient was asked whether he or she had any problems with six IADLs (walking two to three blocks, climbing up 10 steps, walking down 10 steps, preparing meals, heavy housework, and shopping). A physical examination included measurement of height and weight. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Medications used daily or almost daily during the prior 30 days were recorded and categorized according to a computerized coding dictionary.[34] Cognition was assessed by administration of the Mini-Mental State Examination (MMSE) and cognitive impairment was defined as an MMSE score ≤ 24.[35]

Statistical Analyses

Differences in the characteristics of the participants at baseline and follow-up according to level of depressive symptoms were assessed using a chi-square test for categorical variables, analysis of variance for normally distributed continuous data, and Kruskal-Wallis tests for skewed continuous data (caffeine intake and number of medical conditions). Covariates (baseline values) were included in multivariable models if they were known correlates of sleep disturbance or depression or if they were related to the level of depressive symptoms at follow-up in this population ($P \leq 0.10$). These included age, race, site, smoking status, alcohol intake, BMI, self-reported health status, education, exercise, reported number of medical conditions, IADLs, antidepressant use, use of nonbenzodiazepine anxiolytic medications, use of medications for sleep, and baseline GDS score.

Separate logistic regression models were used first to estimate the odds ratio (OR) (95% CI) for falling into different depressive symptom level categories (i.e., "some depressive symptoms" (GDS 3-5) or "depressed" (GDS ≥ 6) at follow-up. Logistic regression models were then also used to estimate OR (95% CI) for having a two-point or greater increase in GDS score at follow-up. Models were adjusted for age and site and for multiple variables.

RESULTS

Characteristics of the Study Population

A schematic of recruitment and inclusion of women in this analysis is shown in Figure 1. The final group of 952 included women differed from the rest of the women participating in the SOF study at baseline in several ways. The mean age was slightly younger (82.5 versus 84.15 y, P < 0.001). They were less likely to report use of antidepressant medications (7.26% versus 17.09%, P < 0.001). They reported fewer medical conditions (2.09 ± 1.45 versus 2.59 ± 1.67, P < 0.001) and their

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Table 1—Characteristics of participants according to level of depressive symptoms at follow-up.

Population Characteristics	All Participants	Level of Depressive Symptoms			P-value
		Normal (GDS 0-2)	Some Depressive Symptoms (GDS 3-5)	Depressed (GDS ≥ 6)	
Total number of participants	952	702	204	46	
Age group n (%)					0.224
70-80	214 (22.48)	168 (23.93)	37 (18.14)	9 (19.57)	
81-82	324 (34.03)	245 (34.90)	67 (32.84)	12 (26.09)	
83-85	256 (26.89)	183 (26.07)	58 (28.43)	15 (32.61)	
86-100	158 (16.6)	106 (15.10)	42 (20.59)	10 (21.74)	
African-American, n (%)	110 (11.55)	83 (11.82)	18 (8.82)	9 (19.57)	0.109
Self-reported health status, n (%)					< 0.001
Excellent or good	838 (88.03)	635 (90.46)	168 (82.35)	35 (76.09)	
Fair, poor, or very poor	114 (11.97)	67 (9.54)	36 (17.65)	11 (23.91)	
Lives alone, n (%)	560 (58.82)	419 (59.69)	117 (57.35)	24 (52.17)	0.539
Education, n (%)					0.009
Less than high school diploma	147 (15.44)	94 (13.39)	40 (19.61)	13 (28.26)	
High school diploma	412 (43.28)	301 (42.88)	92 (45.1)	19 (41.30)	
College/Graduate School	393 (41.28)	307 (43.73)	72 (35.29)	14 (30.43)	
Alcohol use (Drinks per week) n (%)					0.104
0-2 drinks per week	827 (86.87)	601 (85.61)	183 (89.71)	43 (93.48)	
3-13 drinks per week	107 (11.24)	89 (12.68)	15 (7.35)	3 (6.52)	
> 13 drinks per week	18 (1.89)	12 (1.71)	6 (2.94)		
Smoking status, n(%)					0.956
Never Smoked	640 (67.23)	472 (67.24)	139 (68.14)	29 (63.04)	
Former Smoker	292 (30.67)	216 (30.77)	60 (29.41)	16 (34.78)	
Current Smoker	20 (2.10)	14 (1.99)	5 (2.45)	1 (2.17)	
Caffeine intake, mean ± SD, mg/day	161.05 ± 158.36	157.36 ± 158.52	173.58 ± 159.63	161.63 ± 150.6	0.275
Current antidepressant use, n (%)	69 (7.26)	43 (6.13)	24 (11.76)	2 (4.35)	0.018
Current benzodiazepine use, n (%)	50 (5.26)	37 (5.28)	12 (5.88)	1 (2.17)	0.595
Current non-benxodiaxepine anxiolytic/hypnotic use n (%)	7 (0.74)	2 (0.29)	4 (1.96)	1 (2.17)	0.024
Reported use of sleep medication, n (%)	120 (12.62)	86 (12.27)	28 (13.73)	6 (13.04)	0.855
Cognitively impaired (MMSE < 24), n (%)	19 (2.05)	10 (1.45)	8 (4.15)	1 (2.33)	0.065
Body mass index (BMI), n (%)					0.219
Underweight or normal weight (BMI < 25)	308 (32.46)	226 (32.33)	67 (32.84)	15 (32.61)	
Overweight (BMI 25-30)	388 (40.89)	298 (42.63)	76 (37.25)	14 (30.43)	
Obese (BMI ≥ 30)	253 (26.66)	175 (25.04)	61 (29.90)	17 (36.96)	
Takes walks for exercise, n (%)	423 (44.81)	328 (47.06)	79 (39.30)	16 (34.78)	0.056
IADL impairments, n (%)	367 (38.67)	239 (34.09)	104 (51.49)	24 (52.17)	< 0.001
Number of selected medical conditions,* mean ± SD	2.09 ± 1.45	2.03 ± 1.43	2.28 ± 1.52	2.15 ± 1.41	0.141

There were significant associations between level of depressive symptoms at follow up and several covariates including age, self-reported health status, education, alcohol use, exercise, IADL impairment, number of reported medical conditions, and use of antidepressants and nonbenzodiazepine anxiolytic/hypnotic medications. *Reported medical conditions included stroke, diabetes, Parkinson disease, chronic obstructive pulmonary disease, congestive heart failure, myocardial infarction, thyroid disease, hypertension, other neurological condition, other cardiac condition, osteoarthritis, rheumatoid arthritis, osteoporosis, and cancer. BMI, body mass index; IADL, instrumental activities of daily living; MMSE, Mini-Mental State Examination.

average subjective sleep quality was slightly better (PSQI 5.89 ± 3.4 versus 6.35 ± 3.74, P < 0.001). They were more likely to be obese, more educated, to report exercise, and to report their health as good and less likely to be cognitively impaired or report impairment in IADLs.

The characteristics of the population analyzed at follow-up are shown in Table 1. The mean time between baseline and follow-up assessments was 4.91 ± 0.58 y. Most of the women in the analysis were Caucasian, 80 y or older, and were not cognitively impaired. More than 85% of the study population reported their health status to be "excellent" or "good" and

reported drinking less than two alcoholic beverages per week. A minority of women reported use of antidepressants, or medications for sleep. Poorer self-reported health, fewer years of education, more reported impairment in IADLs, and reported use of antidepressants or nonbenzodiazepine anxiolytics were associated with level of depressive symptoms at follow-up.

Associations Between Subjective Measures and Level of Depressive Symptoms at Follow-up

In base models, poorer sleep quality, defined as each standard deviation increase in baseline PSQI score, was associated

Table 2—Associations between subjective sleep disturbances at baseline and depressive symptom level at follow-up

Baseline Subjective Sleep Measure	Some Depressive Symptoms (GDS 2-5) Odds Ratios (95% CI)	P-value	Depressed (GDS ≥ 6) Odds Ratios (95% CI)	P-value
Pittsburgh Sleep Quality Index (PSQI) Total Score				
Base model	1.25 (1.07-1.45)	0.004	1.28 (0.97-1.70)	0.086
Multivariable adjusted	1.14 (0.96-1.35)	0.149	1.13 (0.81-1.58)	0.463
Subjective Poor Sleep (PSQI > 5 vs. PSQI ≤ 5)				
Base model	1.27 (0.93-1.73)	0.135	1.62 (0.88-2.96)	0.119
Multivariable adjusted	1.06 (0.75-1.49)	0.753	1.28 (0.66-2.47)	0.462
Sleep Quality Subcomponent				
Base model	1.50 (1.2-1.87)	< 0.001	1.34 (0.89-2.02)	0.158
Multivariable adjusted	1.37 (1.07-1.75)	0.012	1.20 (0.75-1.92)	0.454
Sleep Latency Subcomponent				
Base model	1.23 (1.05-1.45)	0.009	1.06 (0.78-1.44)	0.692
Multivariable adjusted	1.16 (0.98-1.35)	0.085	0.95 (0.69-1.31)	0.746
Sleep Duration Subcomponent				
Base model	1.14 (0.93-1.41)	0.214	1.19 (0.80-1.77)	0.387
Multivariable adjusted	1.08 (0.87-1.38)	0.496	1.03 (0.69-1.53)	0.887
Sleep Efficiency Subcomponent				
Base model	1.10 (0.95-1.27)	0.191	1.21 (0.93-1.59)	0.155
Multivariable adjusted	1.01 (0.86-1.18)	0.891	1.08 (0.81-1.43)	0.618
Sleep Disturbances Subcomponent				
Base model	1.40 (1.01-1.95)	0.045	1.90 (1.06-3.41)	0.033
Multivariable adjusted	1.21 (0.86-1.71)	0.268	1.64 (0.89-3.02)	0.114
Sleep Medication Use Subcomponent				
Base model	0.97 (0.83-1.14)	0.703	1.00 (0.73-1.36)	0.997
Multivariable adjusted	0.88 (0.71-1.09)	0.249	0.97 (0.65-1.46)	0.882
Daytime Dysfunction Subcomponent				
Base model	1.66 (1.25-2.20)	< 0.001	1.86 (1.11-3.13)	0.019
Multivariable adjusted	1.34 (0.98-1.83)	0.064	1.62 (0.90-2.93)	0.110

Odds ratios and 95% confidence intervals for falling into the "some depressive symptoms" or "depressed" groups at follow-up are given according to baseline subjective sleep measures. For PSQI, total score odds are given for each standard deviation (3.4 points) increase in score. For PSQI subcomponent scores, odds are given per 1-point increase in score. Base models were adjusted for age and site. Multivariable models were adjusted for age, race, site, smoking status, alcohol use, self-reported health status, education, body mass index, reported walking for exercise, number of reported medical conditions, impairments in instrumental activities of daily living, and use of antidepressants, nonbenzodiazepine anxiolytic medications, medications for sleep, and baseline GDS score. CI, confidence interval; GDS, Geriatric Depression Scale; PSQI, Pittsburgh Sleep Quality Index.

with 1.25-fold increased odds of falling into the "some depressive symptoms" group at follow-up as well as a nonstatistically significant 1.28-fold greater odds of being "depressed" at follow-up (Table 2). However, neither association was statistically significant in multivariate models. We did not observe a significant association between poor subjective sleep quality, defined as PSQI > 5, and level of depressive symptoms at follow-up.

In base models there were also significant associations between having higher baseline scores on the sleep quality, sleep latency, sleep disturbances, and daytime dysfunction PSQI subcomponents and increased odds (1.2-1.9 fold) and follow-up depression symptom categories (Table 2). In multivariate models, the associations were attenuated and remained significant only for the sleep quality PSQI subcomponent and the "some depressive symptoms group."

A three-factor strategy for grouping PSQI subcomponents was also used.[36] In base models there were significant associations between greater daily disturbances (i.e., sleep disturbances + daytime dysfunction) subscale scores and greater odds of falling into the "some depressive symptoms" (OR 1.43,

CI 1.18-1.74, P < 0.001) or "depressed" group (OR 1.65, CI 1.17-2.32, P = 0.004) at follow-up. There was also a significant association between greater perceived sleep quality scores (i.e., sleep quality + sleep latency + sleep medication use) and greater odds of falling into the "some depressive symptoms" category at follow-up. In multivariate models the associations between the three-factor daily disturbances and falling into the "some depressive symptoms" (OR 1.24, CI 1.06-1.53, P = 0.051) or the "depressed" (OR 1.50, CI 1.02-2.20, P = 0.040) groups at follow-up were attenuated, whereas the association between greater perceived sleep quality score and greater odds of falling into the "some depressive symptoms" category was not significant.

Associations Between Baseline Subjective Sleep Measures and Odds of Increased Depressive Symptoms at Follow-up

Overall the mean change in GDS score between baseline and follow-up was 0.97 ± 1.73 points. Approximately 50% of women endorsed more depressive symptoms at follow-up (range 1-10 more points on the GDS) and about 25% of women

Table 3—Associations between subjective sleep measures at baseline and worsening depressive symptoms

Baseline Subjective Sleep Measure	≥ 2 Point Increase in GDS Odds Ratio (95% CI)	P-value
Pittsburgh Sleep Quality Index (PSQI) Total Score		
Base model	1.21 (1.05-1.39)	0.007
Multivariable adjusted	1.19 (1.01-1.40)	0.036
Poor Subjective Sleep Quality (PSQI > 5 vs. ≤ 5)		
Base model	1.31 (0.99-1.74)	0.062
Multivariable adjusted	1.28 (0.94-1.75)	0.118
Sleep Quality Subcomponent		
Base model	1.44 (1.18-1.77)	< 0.001
Multivariable adjusted	1.41 (1.13-1.77)	0.003
Sleep Latency Subcomponent		
Base model	1.23 (1.06-1.42)	0.006
Multivariable adjusted	1.21 (1.03-1.41)	0.018
Sleep Duration Subcomponent		
Base model	1.08 (0.89-1.31)	0.426
Multivariable adjusted	1.08 (0.88-1.33)	0.448
Sleep Efficiency Subcomponent		
Base model	1.10 (0.96-1.25)	0.179
Multivariable adjusted	1.05 (0.91-1.21)	0.509
Sleep Disturbances Subcomponent		
Base model	1.36 (1.00-1.84)	0.785
Multivariable adjusted	1.28 (0.93-1.77)	0.125
Sleep Medication Use Subcomponent		
Base model	1.02 (0.88-1.18)	0.048
Multivariable adjusted	0.93 (0.77-1.13)	0.474
Daytime Dysfunction Subcomponent		
Base model	1.24 (0.96-1.59)	0.098
Multivariable adjusted	1.29 (0.98-1.70)	0.075

Odds ratios and 95% confidence intervals for worsening depressive symptoms (≥ 2 point increase in GDS score between baseline and follow-up) according to baseline subjective sleep quality measure. For PSQI total score, odds are given for each standard deviation (3.4 points) increase in PSQI total score. For PSQI subcomponent scores, odds are given per 1-point increase in score. Base models were adjusted for age and site. Multivariable models were adjusted for age, race, site, smoking status, alcohol use, self-reported health status, education, body mass index, reported walking for exercise, number of reported medical conditions, impairments in instrumental activities of daily living, and use of antidepressants, non-benzodiazepine anxiolytic medications, medications for sleep, and baseline GDS score. CI, confidence interval; GDS, Geriatric Depression Scale; PSQI, Pittsburgh Sleep Quality Index.

endorsed a ≥ 2-point increase in depressive symptoms. Approximately 10% of women endorsed fewer depressive symptoms at follow-up (1-2 points less on the GDS).

For each standard deviation (3.4 points) increase in PSQI total score at baseline (i.e., worse sleep quality), there was a 1.2-fold increase in the odds for worsening depressive symptoms in both base and multivariate models (Table 3). In contrast, there was no significant association between poor subjective sleep quality, defined by the cutoff score PSQI > 5, and worsening depressive symptoms at follow-up (Table 3).

For each 1-point increase in the sleep quality PSQI subcomponent score, there was a significant 1.4-fold increase in odds for worsening depressive symptoms. Similarly, for each 1-point increase in the sleep latency PSQI subcomponent score, there was a significant 1.2-fold increase in odds for worsening depressive symptoms. These associations remained significant in multivariate models (Table 3).

Using the three-factor strategy for grouping PSQI subcomponents,[36] there was a significant association between increased three-factor daily disturbances (i.e., sleep disturbances + daytime dysfunction) scores and greater odds of having more depressive symptoms at follow-up (MOR 1.24, CI 1.02-1.50, P < 0.030). There was also a significant association between increased 3-factor perceived sleep latency (i.e., sleep quality + sleep latency + sleep medication use) scores and having more depressive symptoms at follow-up (MOR 1.11, CI 1.03-1.19, P = 0.006).

Associations Between Baseline Objective Sleep Disturbances and Depressive Symptoms at Follow-up

Baseline objectively measured WASO ≥ 60 min was associated with 1.5-fold increased odds having "some depressive symptoms" at follow-up in base models (Table 4). However, this association was attenuated and no longer significant in multivariate models. There was a significant association between baseline WASO ≥ 60 min and a 1.4-fold increased odds worsening depressive symptoms at follow-up in base models (Table 5). This association remained significant and was only slightly attenuated in multivariate models. In contrast, there were no associations between other objectively measured sleep disturbances and either level of depressive symptom or increase in GDS score at follow-up.

Additional Analyses

To explore the role of antidepressants in the longitudinal relationship between sleep disturbances and depressive symptoms further, we examined interactions between the sleep disturbances and antidepressant use in all multivariate models. There was a significant interaction between WASO ≥ 60 min and antidepressant use (P = 0.024) in the model predicting "more depressive symptoms" as an outcome but not between other sleep disturbances and antidepressant use in any model tested.

DISCUSSION

In this group of community-dwelling older women with few or no depressive symptoms at baseline, poorer subjective sleep quality or having objective evidence of sleep fragmentation at baseline was associated with increased risk of worsening depressive symptoms between baseline and follow-up approximately 5 y later.

These results add to the growing body of literature suggesting that subjective sleep disturbance increases risk for depression.[17,18,20,21,37,38] Studies in younger adults have suggested the

Table 4—Associations between baseline objective sleep disturbances and level of depressive symptoms at follow-up

Baseline Sleep Disturbance	Some Depressive Symptoms (GDS 2-5) Odds Ratio (95% CI)	P-value	Depressed (GDS ≥ 6) Odds Ratio (95% CI)	P-value
Sleep Efficiency < 85% vs. ≥ 85%				
Base model	1.11 (0.80-1.55)	0.539	1.20 (0.63-2.29)	0.585
Multivariable adjusted	1.09 (0.76-1.55)	0.645	0.95 (0.48-1.92)	0.895
Sleep Onset Latency ≥ 60 minutes vs. < 60 minutes				
Base model	0.98 (0.63-1.53)	0.937	1.37 (0.64-2.93)	0.420
Multivariable adjusted	0.85 (0.53-1.36)	0.495	1.03 (0.46-2.32)	0.940
Wake After Sleep Onset ≥ 60 minutes < 60 minutes				
Base model	1.49 (1.09-2.04)	0.014	0.96 (0.53-1.76)	0.902
Multivariable adjusted	1.33 (0.95-1.86)	0.095	0.72 (0.37-1.37)	0.310
> 8 Long Wake Episodes vs. ≥ 8 Long Wake Episodes				
Base model	1.36 (0.95-1.96)	0.097	1.00 (0.48-2.06)	0.994
Multivariable adjusted	1.25 (0.85-1.84)	0.267	0.82 (0.38-1.77)	0.607
Total Sleep Time < 5 hours (short sleeper) vs 5-8 hours (normal sleeper)				
Base model	0.88 (0.44-1.76)	0.724	2.13 (0.78-5.81)	0.140
Multivariable adjusted	0.69 (0.33-1.47)	0.341	1.66 (0.56-4.92)	0.357
Total Sleep Time > 8 hours (long sleeper) vs 5-8 hours (normal sleeper)				
Base model	0.90 (0.55-1.48)	0.684	1.76 (0.78-3.95)	0.171
Multivariable adjusted	0.81 (0.48-1.36)	0.418	1.80 (0.77-4.20)	0.177

Odds ratios and 95% confidence intervals for falling into the "some depressive symptoms" or "depressed" groups at follow-up are given according to baseline objective sleep disturbance. Base models were adjusted for age and site. Multivariable models were adjusted for age, race, site, smoking status, alcohol use, self-reported health status, education, body mass index, reported walking for exercise, number of reported medical conditions, impairments in instrumental activities of daily living, and use of antidepressants, nonbenzodiazepine anxiolytic medications, medications for sleep, and baseline GDS score. CI, confidence interval; GDS, Geriatric Depression Scale; PSQI, Pittsburgh Sleep Quality Index.

odds of future depression are increased twofold to fourfold for those with subjective disturbances in sleep at baseline.[17,21,37,38] Few studies have examined this relationship in older adults. One study found that subjective sleep disturbance at baseline increased odds of endorsing significant depressive symptoms at follow-up, approximately 2.3 years later, by 3.2-fold[18] compared to 1.2-fold increased odds in our study. This discrepancy could be because of the differences in follow-up time periods, as the follow-up period was longer (approximately 5 y) in the current study, or sample populations, as the latter study included men and women who were younger than 80 y whereas the current study consisted entirely of women, most of whom were older than 80 y.

Few studies have looked at the relationship between objective sleep measures and depressive symptoms in older adults. We previously reported a moderate cross-sectional association between objective (assessed by actigraphy) evidence of increased fragmentation of sleep as defined by WASO ≥ 60 min in this cohort and greater levels of depressive symptoms.[23] Here we report that, in women who are not depressed at baseline, having WASO ≥ 60 min increased odds of having worsening depressive symptoms over the next 5 y by approximately 1.4-fold even in multivariate models including adjustment for baseline depressive symptoms. To our knowledge, this is the first study to report an independent longitudinal relationship between objectively measured fragmentation of sleep and depressive symptoms in older adults. A similar longitudinal study in a large cohort of older men recently found strong associations between worse subjectively measured sleep quality at

baseline and more depressive symptoms at follow-up approximately 3.4 y later. In that study, several baseline objectively assessed (by actigraphy) sleep disturbances were associated with greater levels of depressive symptoms at follow-up in base models; however, these associations were attenuated and no longer significant after models were adjusted for baseline depressive symptoms, suggesting that the associations were largely explained by a greater burden of depressive symptoms at baseline in the men with the sleep disturbances.[39] The difference between these findings and ours may be related to the sex or age of the cohorts because our study included participants who were female and who were older compared with the men in that cohort. It is notable that the association between WASO ≥ 60 min and increased depressive symptoms was only observed in our secondary analysis examining odds of endorsing a two-point or greater increase in GDS score over time, which was not a strategy used to examine this relationship in the older men. In our primary analysis, no significant association between WASO ≥ 60 min and increased level depressive symptoms was observed. Hence, these findings require verification in other cohorts.

Greater baseline score on the sleep latency PSQI subcomponent, but not baseline objectively measured prolonged sleep latency, was associated with increased risk for endorsing more depressive symptoms at follow-up. It is possible that actigraphy was not able to detect a subtle or qualitative difference in sleep latency that was appreciated subjectively by the women. The literature regarding the ability of actigraphy to accurately assess SOL has been mixed,[40,41] and actigraphy is unable to detect with

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Table 5—Associations between objective sleep disturbances at baseline and worsening depressive symptoms

Sleep Disturbance at Baseline	≥ 2 Point Increase in GDS Odds Ratio (95% CI)	P-value
Sleep Efficiency < 85% vs. ≥ 85%		
Base model	1.09 (0.81-1.47)	0.583
Multivariable adjusted	1.04 (0.76-1.43)	0.812
Sleep Onset Latency ≥ 60 minutes vs. < 60 minutes		
Base model	0.96 (0.64-1.44)	0.845
Multivariable adjusted	0.90 (0.59-1.38)	0.641
Wake After Sleep Onset ≥ 60 minutes < 60 minutes		
Base model	1.42 (1.06-1.88)	0.017
Multivariable adjusted	1.36 (1.01-1.84)	0.046
> 8 Long Wake Episodes vs. ≥ 8 Long Wake Episodes		
Base model	1.33 (0.95-1.85)	0.098
Multivariable adjusted	1.24 (0.87-1.77)	0.235
Total Sleep Time < 5 hours (short sleeper) vs. 5-8 hours (normal sleeper)		
Base model	0.87 (0.46-1.64)	0.663
Multivariable adjusted	0.84 (0.43-1.63)	0.602
Total Sleep Time > 8 hours (long sleeper) vs. 5-8 hours (normal sleeper)		
Base model	1.43 (0.94-2.17)	0.095
Multivariable adjusted	1.33 (0.86-2.05)	0.202

Odds ratios and 95% confidence intervals for a two or worsening depressive symptoms (≥ 2 point increase in GDS score) are given for women with subjective and objective sleep disturbances at baseline compared to those without. Base models were adjusted for age and site. Multivariable models were adjusted for age, race, site, smoking status, alcohol use, self-reported health status, education, body mass index, reported walking for exercise, number of reported medical conditions, impairments in instrumental activities of daily living, and use of antidepressants, nonbenzodiazepine anxiolytic medications, medications for sleep, and baseline GDS score. CI, confidence interval; GDS, Geriatric Depression Scale; PSQI, Pittsburgh Sleep Quality Index.

certainty the transition between quiet wakefulness preceding sleep and sleep. Studies using other methods of objective sleep assessment, such as PSG, would be useful to further evaluate this relationship.

The association between a higher sleep quality PSQI subcomponent score and future endorsement of "some depressive symptoms" in multivariate models suggests that in older women without depression, subjective complaints about sleep quality may increase risk for subthreshold levels of depressive symptoms. In older adults, subthreshold depressive syndromes are almost twice as common as major depression,[2,5–7] representing a majority of depressive syndromes experienced in this age group. Subthreshold depression is a serious condition in older adults associated with adverse outcomes in older adults,[42] including functional impairment,[11] increased disability burden[14] increased risk of physical decline,[43] and increased risk for developing major depression.[5] Attention is therefore warranted to increasing knowledge about these syndromes and developing treatment interventions for them.[44]

This study has several strengths. The sample size is large, collected from three separate geographic locations, and the women were not selected based on depressive symptoms or on their report of sleep disturbances. Unlike most previous studies examining the longitudinal relationship between sleep disturbances and depressive symptoms in older adults, both subjective and objective measures of sleep disturbance at baseline

were assessed. There are several limitations to this analysis. Our analysis was designed to make use of data that were collected as part of a larger study. Hence, the study was not designed to answer our hypothesis and outcome measures were not predefined. The sample is made up of community-dwelling women age 70 y and older, most of whom were white and older than 80 y, and the findings therefore may not be applicable to other populations. We intentionally selected women for this analysis who had few or no depressive symptoms at baseline, likely excluding many women with more chronic or severe depressive syndromes. This aspect of the study design may have limited our ability to detect associations between sleep disturbances and depressive symptoms. Depressive symptoms were assessed by questionnaire rather than a clinical diagnostic interview, and so conclusions about psychiatric diagnosis cannot be made. Although it has been well validated in multiple age groups, unlike PSG, the gold standard tool for the assessment of sleep and sleep disruption, actigraphy cannot definitively determine whether the participant is sleeping or awake. Quiet wakefulness can be mistaken for sleep, an error that would affect measurement for participants who sleep poorly to a greater degree than those who sleep normally. This could potentially result in an underestimation of WASO in poor sleepers and potentially an underestimation of the relationship between WASO ≥ 60 min and depressive symptoms. Actigraphy also relies on self-reported times in and out of bed, which may be inaccurate and could introduce errors into measurements such as sleep onset latency.

In conclusion, both subjective sleep disturbance and objective evidence of sleep fragmentation increased risk for worsening depressive symptoms in a cohort of community- dwelling older women who did not endorse significant depressive symptoms at baseline.

REFERENCES

1. Borson S, Barnes RA, Kukull WA, et al. Symptomatic depression in elderly medical outpatients. I. Prevalence, demography, and health service utilization. J Am Geriatr Soc 1986;34:341–7.
2. Lyness JM, King DA, Cox C, Yoediono Z, Caine ED. The importance of subsyndromal depression in older primary care patients: prevalence and associated functional disability. J Am Geriatr Soc 1999;47:647–52.
3. Schulberg HC, Mulsant B, Schulz R, Rollman BL, Houck PR, Reynolds CF, 3rd. Characteristics and course of major depression in older primary care patients. Int J Psychiatry Med 1998;28:421–36.
4. Steffens DC, Skoog I, Norton MC, et al. Prevalence of depression and its treatment in an elderly population: the Cache County study. Arch Gen Psychiatry 2000;57:601–7.
5. Judd LL, Akiskal HS. The clinical and public health relevance of current research on subthreshold depressive symptoms to elderly patients. Am J Geriatr Psychiatry 2002;10:233–8.
6. Judd LL, Akiskal HS, Maser JD, et al. A prospective 12-year study of subsyndromal and syndromal depressive symptoms in unipolar major depressive disorders. Arch Gen Psychiatry 1998;55:694–700.
7. Judd LL, Akiskal HS, Maser JD, et al. Major depressive disorder: a prospective study of residual subthreshold depressive symptoms as predictor of rapid relapse. J Affect Disord 1998;50:97–108.
8. Olfson M, Broadhead WE, Weissman MM, et al. Subthreshold psychiatric symptoms in a primary care group practice. Arch Gen Psychiatry 1996;53:880–6.
9. Adams KB, Moon H. Subthreshold depression: characteristics and risk factors among vulnerable elders. Aging Ment Health 2009;13:682–92.
10. Bruce ML. Depression and disability in late life: directions for future research. Am J Geriatr Psychiatry 2001;9:102–12.
11. Lyness JM, Kim J, Tang W, et al. The clinical significance of subsyndromal depression in older primary care patients. Am J Geriatr Psychiatry 2007;15:214–23.
12. Frasure-Smith N, Lesperance F. Depression--a cardiac risk factor in search of a treatment. JAMA 2003;289:3171–3.
13. Alexopoulos GS, Vrontou C, Kakuma T, et al. Disability in geriatric depression. Am J Psychiatry 1996;153:877–85.
14. Cronin-Stubbs D, de Leon CF, Beckett LA, Field TS, Glynn RJ, Evans DA. Six-year effect of depressive symptoms on the course of physical disability in community-living older adults. Arch Intern Med 2000;160:3074–80.
15. Whooley MA, Browner WS. Association between depressive symptoms and mortality in older women. Study of Osteoporotic Fractures Research Group. Arch Intern Med 1998;158:2129–35.
16. Unutzer J, Patrick DL, Simon G, et al. Depressive symptoms and the cost of health services in HMO patients aged 65 years and older. A 4-year prospective study. JAMA 1997;277:1618–23.
17. Franzen PL, Buysse DJ. Sleep disturbances and depression: risk relationships for subsequent depression and therapeutic implications. Dialogues Clin Neurosci 2008;10:473–81.
18. Livingston G, Blizard B, Mann A. Does sleep disturbance predict depression in elderly people? A study in inner London. Br J Gen Pract 1993;43:445–8.
19. Perlis ML, Smith LJ, Lyness JM, et al. Insomnia as a risk factor for onset of depression in the elderly. Behav Sleep Med 2006;4:104–13.
20. Roberts RE, Shema SJ, Kaplan GA, Strawbridge WJ. Sleep complaints and depression in an aging cohort: A prospective perspective. Am J Psychiatry 2000;157:81–8.
21. Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. Biol Psychiatry 1996;39:411–8.
22. Paudel ML, Taylor BC, Diem SJ, et al. Association between depressive symptoms and sleep disturbances in community-dwelling older men. J Am Geriatr Soc 2008;56:1228–35.
23. Maglione JE, Ancoli-Israel S, Peters KW, et al. Depressive symptoms and subjective and objective sleep in community-dwelling older women. J Am Geriatr Soc 2012;60:635–43.
24. Cummings SR, Black DM, Nevitt MC, et al. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. Lancet 1993;341:72–5.
25. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193–213.
26. Blackwell T, Ancoli-Israel S, Gehrman PR, Schneider JL, Pedula KL, Stone KL. Actigraphy scoring reliability in the study of osteoporotic fractures. Sleep 2005;28:1599–605.
27. Blackwell T, Redline S, Ancoli-Israel S, et al. Comparison of sleep parameters from actigraphy and polysomnography in older women: the SOF study. Sleep 2008;31:283–91.
28. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. Sleep 2003;26:342–92.
29. Cole RJ, Kripke DF, Gruen W, Mullaney DJ, Gillin JC. Automatic sleep/wake identification from wrist activity. Sleep 1992;15:461–9.
30. Jean-Louis G, Kripke DF, Mason WJ, Elliott JA, Youngstedt SD. Sleep estimation from wrist movement quantified by different actigraphic modalities. J Neurosci Methods 2001;105:185–91.
31. Brink TL. Clinical gerontology: a guide to assessment and intervention. New York: Howarth Press, 1986.
32. Almeida OP, Almeida SA. Short versions of the geriatric depression scale: a study of their validity for the diagnosis of a major depressive episode according to ICD-10 and DSM-IV. Int J Geriatr Psychiatry 1999;14:858–65.
33. Barone JJ, Roberts HR. Caffeine consumption. Food Chem Toxicol 1996;34:119–29.
34. Pahor M, Chrischilles EA, Guralnik JM, Brown SL, Wallace RB, Carbonin P. Drug data coding and analysis in epidemiologic studies. Eur J Epidemiol 1994;10:405–11.
35. 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;12:189–98.
36. Cole JC, Motivala SJ, Buysse DJ, Oxman MN, Levin MJ, Irwin MR. Validation of a 3-factor scoring model for the Pittsburgh sleep quality index in older adults. Sleep 2006;29:112–6.
37. Buysse DJ, Angst J, Gamma A, Ajdacic V, Eich D, Rossler W. Prevalence, course, and comorbidity of insomnia and depression in young adults. Sleep 2008;31:473–80.
38. Chang PP, Ford DE, Mead LA, Cooper-Patrick L, Klag MJ. Insomnia in young men and subsequent depression. The Johns Hopkins Precursors Study. Am J Epidemiol 1997;146:105–14.
39. Paudel M, Taylor BC, Ancoli-Israel S, et al. Sleep disturbances and risk of depression in older men. Sleep 2013;36:1033–40.
40. Martin JL, Hakim AD. Wrist actigraphy. Chest 2011;139:1514–27.
41. Sadeh A. The role and validity of actigraphy in sleep medicine: an update. Sleep Med Rev 2011;15:259–67.
42. Grabovich A, Lu N, Tang W, Tu X, Lyness JM. Outcomes of subsyndromal depression in older primary care patients. Am J Geriatr Psychiatry 2010;18:227–35.
43. Penninx BW, Guralnik JM, Ferrucci L, Simonsick EM, Deeg DJ, Wallace RB. Depressive symptoms and physical decline in community-dwelling older persons. JAMA 1998;279:1720–6.
44. Meeks TW, Vahia IV, Lavretsky H, Kulkarni G, Jeste DV. A tune in "a minor" can "b major": a review of epidemiology, illness course, and public health implications of subthreshold depression in older adults. J Affect Disord 2011;129:126–42.