Title

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Journal

Journal of Gerontology Series B: Psychological Sciences and Social Sciences, 70(5)

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Publication Date

2015-09-01

DOI

10.1093/geronb/gbt125

Peer reviewed

THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Psychological Sciences
cite as: *J Gerontol B Psych Sci Soc Sci*, 2015, Vol. 70, No. 5, 673–681
doi:10.1093/geronb/gbt125
Advance Access publication December 10, 2013

OXFORD

Original Research Report

Sleep Architecture and Mental Health Among Community-Dwelling Older Men

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Received June 25 2013; Accepted November 6 2013.

Decision Editor: Bob G. Knight, PhD

Abstract

Objectives. To investigate the association of mood and anxiety symptoms with sleep architecture (the distribution of sleep stages) in community-dwelling older men.

Method. We used in-home unattended polysomnography to measure sleep architecture in older men. Men were categorized into 4 mental health categories: (a) significant depressive symptoms only (DEP+ only, Geriatric Depression Scale ≥ 6), (b) significant anxiety symptoms only (ANX+ only, Goldberg Anxiety Scale ≥ 5), (c) significant depressive and anxiety symptoms (DEP+/ANX+), or (d) no significant depressive or anxiety symptoms (DEP–/ANX–).

Results. Compared with men without clinically significant symptomology, men with depressive symptoms spent a higher percentage of time in Stage 2 sleep (65.42% DEP+ only vs 62.47% DEP–/ANX–, $p = .003$) and a lower percentage of time in rapid eye movement sleep (17.05% DEP+ only vs 19.44% DEP–/ANX–, $p = .0005$). These differences persisted after adjustment for demographic/lifestyle characteristics, medical conditions, medications, and sleep disturbances, and after excluding participants using psychotropic medications. The sleep architecture of ANX+ or DEP+/ANX+ men did not differ from asymptomatic men.

Discussion. Depressed mood in older adults may be associated with accelerated age-related changes in sleep architecture. Longitudinal community-based studies using diagnostic measures are needed to further clarify relationships among common mental disorders, aging, and sleep.

Key Words: Aging—Anxiety—Depression—Epidemiology—Sleep architecture

Sleep architecture refers to the distribution electrophysiologically distinct sleep states that occur in cycles throughout the night. In adulthood, sleep is entered through Stage 1, or light sleep, which is characterized by a low arousal threshold. Next, during Stage 2 sleep, more intense stimuli are needed for arousal. Following Stage 2 is slow wave sleep (SWS), sometimes also referred to as deep sleep. Stages 1, 2, and SWS constitute the phases of non-rapid eye movement (N-REM) sleep, which alternates with rapid eye movement (REM) sleep throughout the night. In REM sleep, brain electrical activity resembles waking electrophysiology. The exact function of these sleep stages remains unknown.

Research has described changes in sleep architecture that occur throughout the life span. The percentage of both SWS and REM sleep decrease with aging (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004; Redline et al., 2004). Research has also linked altered sleep architecture with psychiatric disorders, including major depressive disorder (MDD) and generalized anxiety disorder (GAD). Patients with MDD spend a lesser percentage of sleep time in SWS and a greater percentage of sleep time in REM sleep compared with healthy controls (Kupfer & Foster, 1972). Sleep architecture in MDD is also characterized by shorter times from sleep onset to the first REM sleep period (shortened REM sleep latency) and prolongation of the first REM sleep periods (Peterson & Benca, 2011). Within MDD patients, changes in sleep architecture have also been noted during treatment (Reynolds et al., 1991) and after recovery from depressive episodes (Lee et al., 1993), suggesting that such changes may represent traits and/or scars of depressive illness.

Anxiety disorders have been less consistently associated with alterations in sleep architecture. Some studies of GAD have reported decreases in the percentage of time spent in REM sleep (Fuller, Waters, Binks, & Anderson, 1997) and increases in the percentage of time spent in lighter sleep (Fuller et al., 1997; Papadimitriou & Linkowski, 2005). In a review including six studies of GAD and sleep architecture (Monti & Monti, 2000), all of the examined studies showed that, compared with healthy controls, GAD patients spent less time in REM sleep; however, these differences were only statistically significant in one of the studies. The authors of this review also noted that in half of the studies reviewed, the percentage of time GAD patients spent in SWS was significantly decreased.

Although sleep architecture research has primarily examined middle-aged adults, in the 1990s, research in late-life depression replicated the characteristic sleep architecture changes found among younger adults (Lee et al., 1993; Reynolds et al., 1991). The effect of MDD on sleep architecture is found across adulthood (Gillin et al., 1981) but appears to be more pronounced as age increases (Knowles & MacLean, 1990). Although sleep disturbances are common among elderly individuals with clinically significant anxiety (Kostka & Jachimowicz, 2010), to our knowledge, no information exists regarding the sleep architecture of anxious older persons.

Of importance, both MDD and GAD research has almost exclusively relied on clinical samples of treatment-seeking individuals who attend in-laboratory sleep studies. Participants seeking treatment are likely very different than a broad population-based sample of community-dwelling men. To our knowledge, only one small case–control study of non-treatment-seeking older adults with MDD has been conducted (Vitiello et al., 1990). This study was unable to replicate the previously documented MDD-related differences in sleep architecture, leading these authors to conclude that altered sleep architecture in MDD reported in previous studies may have been related to characteristics of treatment-seeking behavior. To our knowledge, no research has examined anxiety and sleep architecture in a community-based sample.

An important role of epidemiology is completing the clinical picture (Morris, 1957), and population-based research is needed to determine whether the associations of mood and anxiety with sleep architecture observed in a clinical setting are also present in the community (or whether they are only present among the portion of the patient population found in the clinic). We report here the sleep architecture of older community-dwelling men with and without clinically significant depression and anxiety symptoms. Based on previous literature, we hypothesized that individuals with depressive symptoms would spend less of their sleep time in SWS, have shorter REM latencies, and spend a greater percentage of sleep time in REM sleep. We also hypothesized that anxiety symptoms would be related to lower amounts of both REM and SWS. Because depression and anxiety may both be associated with REM sleep, although in opposite directions, we additionally explored associations of co-occurring depression and anxiety symptoms with sleep architecture.

Method

Participants

From March 2000 to April 2002, the parent Osteoporotic Fractures in Men (MrOS) Study recruited 5,994 community-dwelling men who were ≥65 years of age at six clinical centers in the United States (Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Monongahela Valley near Pittsburgh, PA; Portland, OR; and San Diego, CA; Blank et al., 2005; Orwoll et al., 2005). To be eligible to participate, individuals must have been without bilateral hip replacements and able to walk without assistance.

The ancillary MrOS Sleep Study was conducted between December 2003 and March 2005 and included 3,135 participants, which exceeded the target recruitment number of 3,000 men from the parent MrOS Study. Men excluded from this sleep study were: 150 treated for sleep apnea or snoring (use of positive airway pressure therapy, a dental appliance, or oxygen); 349 who had died; 39 who withdrew from participation; 1,997 who refused for diverse personal reasons; and 324 because MrOS Sleep Study recruitment goals had already been met.

Of the 3,135 men who participated in the Sleep Visit, 2,911 have polysomnography (PSG) data. Of these, 2,861 have data for the sleep architecture outcomes. Eight men are missing data on depressive symptoms or anxiety, leaving 2,853 men in this analysis subset. The institutional review boards at each clinic site approved the study, and written informed consent was obtained from all participants.

Measures

Polysomnography

In-home sleep studies using unattended PSG (Safiro, Compumedics, Inc., Melbourne, Australia) were performed. Participants were examined for one night in their own homes to minimize burden. PSG records electrical activity at the scalp, which can be analyzed to determine sleep staging. The recording montage was as follows: C_3/A_2 and C_4/A_1 electroencephalograms (EEG), bilateral electrooculograms, and a bipolar submental electromyogram to determine sleep status; thoracic and abdominal respiratory inductance plethysmography to determine respiratory effort; airflow (by nasal–oral thermocouple and nasal pressure cannula); finger pulse oximetry; lead I electrocardiogram (EKG); body position (mercury switch sensor); and bilateral tibialis leg movements (piezoelectric sensors). Centrally

trained and certified staff members performed home visits for setup of the PSG units. After sensors were placed and calibrated, signal quality and impedance were checked; sensors were repositioned as needed to improve signal quality, replacing electrodes if impedances were greater than 5,000 ohms, using approaches similar to those in the Sleep Health Heart Study (Redline et al., 1998). Staff returned the next morning to collect the equipment and download the data to the Central Sleep Reading Center (Cleveland, OH) to be scored by certified research polysomnologists. PSG data quality was excellent, with a failure rate of less than 4% and with more than 70% of studies graded as being of excellent or outstanding quality.

Sleep stages (REM, Stages 1, 2, and SWS) were scored using standard criteria (Rechtschaffen & Kales, 1968) and included the percentage of sleep time spent in Stage 1, Stage 2, SWS, and REM sleep. Also included was REM latency, which was defined as the number of minutes from sleep onset to the first REM period. The reliability of these measures, determined by rescoring studies over time, indicates that the interscorer reliability (ICC) for the percent of sleep time spent in sleep Stages 1, 2, SWS, and REM were .60, .91, .96, and .94, respectively. Similar, although higher levels of intrascorer reliability were also documented.

Mental health

The Geriatric Depression Scale-15 (GDS), a validated short form (Aikman & Oehlert, 2001; Almeida & Almeida, 1999; Sheikh & Yesavage, 1986) to screen for MDD among older persons (Yesavage et al., 1982), was administered to all participants. The standard cut point of ≥6 was used to define clinically significant depressive symptoms. A cutoff of ≥6 yields a sensitivity of 90.9% and specificity of 64.5% compared with a DSM-IV diagnosis of MDD (Almeida & Almeida, 1999). The Goldberg Anxiety Scale with a cutoff of ≥5 was used to determine the presence of clinically significant anxiety symptoms. This was originally validated with a sensitivity and specificity of 86% and 91%, respectively (Goldberg, Bridges, Duncan-Jones, & Grayson, 1988).

We combined these depression and anxiety scales to create four mutually exclusive categories: significant depressive symptoms only (DEP+), significant anxiety symptoms only (ANX+), both depressive and anxiety symptoms (DEP+/ANX+), or no significant depressive or anxiety symptoms (DEP–/ANX–).

Covariates

Demographic/lifestyle and chronic disease/medication use covariates were selected a priori based on their potential associations with mental health (MH) or sleep architecture.

Demographic/lifestyle

At the Sleep Visit, information on age, study site, race/ethnicity, education, alcohol consumption, and smoking status was obtained. Measurements of body weight and height were made, and body mass index was calculated as weight in kilograms divided by the square of height in meters. Physical activity was measured with the Physical Activity Scale for the Elderly (PASE) Scale (Washburn, Smith, Jette, & Janney, 1993).

Chronic disease/medication use

Previous MrOS research has demonstrated associations between chronic diseases and psychoactive medications with sleep architecture (Blackwell, Yaffe, et al., 2011; Rao et al., 2009), and these variables were considered covariates in our analysis. A history of chronic medical conditions was obtained by self-report, including: stroke, Parkinson's disease, diabetes mellitus, chronic obstructive pulmonary disease, hypertension, congestive heart failure, myocardial infarction, and arthritis (osteoarthritis and rheumatoid arthritis). Cognitive impairment was defined as Modified Mini-Mental State Examination (3MS) score < 80 (Teng & Chui, 1987). Participants were asked to bring in all current medications used within the preceding 30 days. All prescription and nonprescription medications were entered into an electronic database and each medication was matched to its ingredient(s) based on the Iowa Drug Information Service Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA; Pahor et al., 1994). The use of medications known to affect sleep architecture were considered (antidepressants, benzodiazepines, and non-benzodiazepine, non-barbiturate sedative hypnotics).

Sleep covariates

Sleep disturbances were also considered as potential covariates to determine whether associations of sleep architecture and MH were independent of sleep disturbances known to occur more frequently among men with depressed mood (Paudel et al., 2008). Covariates of sleep-disordered breathing (SDB) and nocturnal hypoxemia included the apnea–hypopnea index (AHI) and the percent of time during sleep in which arterial oxygen saturation was below 90% (percentage of sleep time with SaO_2 < 90%). Apnea was defined as complete or near complete cessation of airflow for >10 s, and hypopneas were scored if clear reductions in breathing amplitude (at least 30% below baseline breathing) occurred and lasted >10 s (Berry et al., 2012). In these analyses, only apneas and hypopneas that were associated with a 3% or greater desaturation were included. AHI was calculated as the total number of apneas and hypopneas per hour of sleep.

Although sleep architecture (primary outcome) and SDB (covariate) can be measured directly only using PSG, for increased reliability, other sleep covariates were measured using wrist actigraphy (Ambulatory Monitoring, Inc., Ardsley, NY). Actigraphy devices contain an accelerometer that records motion and can determine sleep activity patterns when worn over several days (Ancoli-Israel et al., 2003). Participants were instructed to wear the actigraph continuously for 5 nights/6 days, removing it only for bathing. They were also asked to keep a sleep log used to aid in editing the actigraphy data. Actigraphy data were collected for an average of 5.2 (± 0.9) 24-hr periods. Actigraphy data were analyzed with ActionW-2 software (Ambulatory Monitoring, Inc., Ardsley, NY). Details of the actigraphy scoring algorithms used in this study have been published elsewhere (Blackwell, Ancoli-Israel, Redline, Stone, & Osteoporotic Fractures in Men Study, 2011). Actigraphy-based sleep estimates used in this analysis are total sleep time (total hours slept while in bed), sleep efficiency (percentage of time participant was sleeping while in bed), and sleep latency (amount of time until onset of sleep, defined as when participant achieved sleep for 20 continuous minutes after getting into bed).

Statistical Analysis

The percentages of time spent in each sleep stage were first summarized across demographic/lifestyle categories as mean ± *SD* and compared using *t* tests or analysis of variance. In the main analysis, we used multivariable linear regression to evaluate whether sleep architecture parameters differed according to MH status (compared with the asymptomatic reference group, DEP–/ANX–). All linear regression comparisons were made first in unadjusted models (Model 1),

then after adjustment for demographic, medical, and medication covariates (Model 2), and in the final model, after adjusting for other sleep measures (Model 3) in order to determine if associations of MH with sleep architecture were independent of these covariates. Results were presented as adjusted means and 95% confidence intervals.

Several sensitivity analyses were conducted to rule out alternative explanations of associations between MH and sleep architecture. Analyses were repeated after excluding individuals using medications (n = 352) that could affect sleep architecture (antidepressants, benzodiazepines, and non-benzodiazepine, non-barbiturate sedative hypnotics). Participants with severe SDB (AHI ≥ 30, n = 497) were excluded because SDB is also known to affect sleep architecture (Redline et al., 2004). We also substituted the GDS definition of depression with a proxy of diagnosis, specifically use of any antidepressant medication (n = 216 or 7.57%); this analysis was designed to examine if men being treated pharmacologically for depression had the same sleep architecture patterns found in men with GDS defined depressed mood overall. A post hoc follow-up analysis was also conducted to confirm that depression results would be sustained with a more stringent GDS threshold that yields higher specificity (GDS ≥ 9, n = 65 or 2.28%; Marc, Raue, & Bruce, 2008). All p values reported were two-sided and all analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, NC). p Values less than .05 were considered statistically significant.

Results

The analysis sample was 90.61% white with an average age of 76.38 (*SD* 5.54) years. In total, 94 (3.29%) participants met the criteria for only DEP+, 165 (5.78%) met criteria for only ANX+, and 89 (3.12%) met criteria for both DEP+ and ANX+, with the rest of the sample (n = 2,505, 87.80%) meeting neither criteria (DEP–/ANX–). On average, the men spent 6.82% ± 4.28% of sleep time in Stage 1, 62.64% ± 9.59% in Stage 2, 11.25% ± 8.99% in SWS, and 19.29% ± 6.56% in REM. On average, it took the men 74.62 ± 43.46 min to the first onset of REM sleep.

Associations of Covariates With Sleep Architecture

There were statistically significant associations with age (in quartiles) across all sleep architecture outcomes except SWS and REM latency (Table 1). Men in older age quartiles spent a greater percentage of sleep time in Stage 1 (p < .0001) and Stage 2 sleep (p = .005) and a lesser percentage in REM sleep (p < .0001). Other demographic/lifestyle factors also associated with sleep architecture can be seen in Table 1; for example, higher physical activity scores (PASE) were associated with a greater percentage of sleep time spent in REM (p = .0001) and with shorter REM latencies (p = .0117).

Main Findings: MH and Sleep Architecture

Multivariable linear regression analysis revealed significant independent associations of depressive symptoms (DEP+) with sleep architecture, whereas no statistically significant associations of sleep architecture and anxiety symptoms (ANX+) or comorbid depressive and anxiety symptoms (DEP+/ANX+) were present after adjustment for covariates (Table 2).

Compared with men without clinically significant depressive or anxiety symptoms, men with clinically significant depressive symptoms spent greater percentage of sleep time in Stage 2 sleep (on average, 62.47% DEP–/ANX– vs 65.42% DEP+) and a smaller percentage of sleep time in REM sleep (on average, 19.44% DEP–/ANX– vs 17.05% DEP+). The association of depressive symptoms with Stage 2 and REM sleep remained statistically significant after adjustments for demographic/lifestyle factors, chronic diseases, and medication use (Model 2), as well as after adjustments for sleep disturbances (Model 3). This pattern of findings was unaltered when repeating analyses excluding men using psychoactive medications (antidepressants, benzodiazepines, and non-benzodiazepine, non-barbiturate sedative hypnotics). When excluding 497 men who had severe SDB, the association of DEP+ with the percentage of time spent in Stage 2 sleep was no longer significant in the fully adjusted model (Model 3: 63.50% DEP+ vs 61.87% DEP–/ANX–, p = .1505), whereas DEP+ was still significantly associated with a lesser percentage of time spent in REM sleep (Model 3: 18.12% DEP+ vs 19.92% DEP–/ANX–, p = .0181).

Men with DEP+/ANX+ spent a smaller percentage of sleep time in REM sleep than DEP–/ANX– men (Model 1); however, this result lost significance after adjustment for demographic/lifestyle factors, chronic diseases, and medication use (Model 2). Compared with their counterparts without clinically significant symptoms, all three MH groups had significantly longer REM latencies (Model 1); these differences were no longer statistically significant after adjustments in Model 2.

Repeating the analyses using antidepressant medication as a proxy for MDD diagnosis yielded similar results; however, using this measure of depression additionally yielded a significantly longer REM latency (Model 3: 111.62 min in antidepressant users without anxiety vs 71.53 min in non-antidepressant users without anxiety, p < .0001). Those using antidepressants with anxiety also had longer REM latency than nonusers of antidepressants (Model 3: 101.64 min vs 71.53 min, respectively, p < .0001). In a post hoc sensitivity analysis, a more stringent cutoff was used for the GDS (≥9) in order to increase specificity compared with a full MDD diagnosis above 90% (Marc et al., 2008). This criterion yielded 26 (0.91%) DEP+/ANX–, 215 (7.54%) DEP–/ANX+, and 39 (1.37%) DEP+/ANX+ participants. In the fully adjusted model, there were no longer significant associations of the percentage of time spent in Stage 2 sleep with any MH category compared with DEP–/ANX–, although men with DEP+/ANX– compared with DEP–/ANX– still spent a smaller percentage of time in REM sleep (p = .034).

Discussion

In this first large-scale population-based study of sleep architecture among community-dwelling older men, we found that participants with depressed mood spent a greater percentage of their sleep time in lighter (Stage 2) sleep. We found that depressed mood was associated with a lower percentage of time spent in REM sleep and with trends toward longer latency from sleep onset to the first REM period. We found no statistically significant associations between sleep architecture and anxiety symptoms.

Our findings differ from previous studies of in-patient sleep patterns. This difference may be interpreted in several ways. First, the biological signatures documented in previous sleep architecture studies may be related to some disease processes highly correlated with treatment-seeking behavior. However, our findings were reproduced when examining participants being treated pharmacologically for depression, indicating that an absence of treatment seeking does not explain differing community- and clinic-based findings. Although clinical samples include more severely depressed individuals than our population-based sample, use of a more extreme cut point for

Table 1. Summary of Sleep Staging and REM Latency by Demographic/Lifestyle Characteristics, Mean ± *SD*

Characteristic	% of time spent in Stage 1 sleep	% of time spent in Stage 2 sleep	% of time spent in slow wave sleep	% of time spent in REM sleep	REM latency (min)
Age, years					
<72 (*n* = 657)	**6.02 ± 3.23**	**62.15 ± 8.80**	11.49 ± 8.31	**20.33 ± 6.05**	73.65 ± 41.78
72 to <76 (*n* = 745)	**6.69 ± 4.03**	**61.92 ± 9.56**	11.47 ± 8.88	**19.92 ± 6.35**	73.60 ± 41.23
76 to <80 (*n* = 650)	**6.82 ± 4.22**	**62.91 ± 10.10**	11.14 ± 9.06	**19.13 ± 6.84**	72.89 ± 41.80
80+ (*n* = 801)	**7.58 ± 5.12**	**63.49 ± 9.77**	10.95 ± 9.56	**17.99 ± 6.71**	77.77 ± 47.83
p Value	**<.0001**	**.0052**	.5828	**<.0001**	.1124
BMI, kg/m^2					
<20 (*n* =27)	**8.95 ± 4.71**	62.12 ± 9.51	**11.31 ± 10.21**	17.61 ± 6.03	**83.44 ± 51.46**
20 to <25 (*n* = 837)	**6.59 ± 4.34**	62.20 ± 9.49	**12.08 ± 9.31**	19.13 ± 6.36	**72.42 ± 43.99**
25 to <30 (*n* = 1,411)	**6.85 ± 4.16**	62.54 ± 9.66	**11.04 ± 8.76**	19.57 ± 6.66	**74.15 ± 42.46**
30+ (*n* = 576)	**6.97 ± 4.47**	63.52 ± 9.57	**10.61 ± 8.95**	18.90 ± 6.61	**78.47 ± 44.41**
p Value	**.0198**	.0782	**.0126**	.0746	**.0471**
Race/ethnicity					
White (*n* = 2,585)	6.79 ± 4.26	**62.56 ± 9.60**	**11.45 ± 9.06**	**19.20 ± 6.55**	75.00 ± 43.28
Black (*n* = 97)	6.63 ± 5.31	**65.02 ± 10.21**	**7.84 ± 7.73**	**20.52 ± 7.28**	71.75 ± 57.16
Other (*n* = 171)	7.33 ± 3.93	**62.45 ± 8.98**	**10.19 ± 8.10**	**20.04 ± 6.19**	70.61 ± 36.65
p Value	.2503	**.045**	**.0001**	**.0455**	.3555
Education					
<High school (*n* = 149)	**7.62 ± 4.85**	**64.34 ± 10.57**	10.86 ± 10.60	**17.17 ± 7.03**	**82.73 ± 52.93**
High school (*n* = 466)	**7.64 ± 4.98**	**63.09 ± 9.99**	10.52 ± 8.44	**18.76 ± 6.89**	**77.92 ± 47.23**
Some college or more (*n* = 2,238)	**6.59 ± 4.06**	**62.43 ± 9.43**	11.43 ± 8.98	**19.54 ± 6.43**	**73.40 ± 41.84**
p Value	**<.0001**	**.0342**	.1187	**<.0001**	**.008**
PASE score					
Quartile 1 (*n* = 711)	7.14 ± 4.46	63.06 ± 10.01	11.47 ± 9.64	**18.33 ± 6.89**	**79.12 ± 49.10**
Quartile 2 (*n* = 713)	6.72 ± 4.09	62.55 ± 10.02	11.26 ± 9.17	**19.47 ± 6.51**	**74.17 ± 45.76**
Quartile 3 (*n* = 715)	6.75 ± 3.98	62.71 ± 9.22	10.94 ± 8.53	**19.59 ± 6.62**	**73.22 ± 39.41**
Quartile 4 (*n* = 714)	6.65 ± 4.57	62.24 ± 9.09	11.34 ± 8.59	**19.77 ± 6.12**	**72.01 ± 38.43**
p Value	.1301	.4342	.7259	**.0001**	**.0117**
Alcohol use (drink/week)					
<1 (*n* = 1,326)	6.71 ± 4.14	62.89 ± 9.72	11.30 ± 9.14	19.11 ± 6.87	74.60 ± 44.78
1–13 (*n* = 1,361)	6.88 ± 4.37	62.48 ± 9.42	11.24 ± 8.88	19.4 ± 6.26	74.50 ± 42.72
14+ (*n* = 154)	7.19 ± 4.81	61.69 ± 10.12	11.27 ± 8.93	19.84 ± 6.36	75.70 ± 39.46
p Value	.3209	.2526	.9861	.2865	.9487
Smoking status					
Never (*n* = 1,127)	6.87 ± 4.28	62.88 ± 9.17	11.00 ± 8.60	19.25 ± 6.51	74.26 ± 45.16
Past (*n* = 1,669)	6.77 ± 4.30	62.45 ± 9.80	11.46 ± 9.20	19.33 ± 6.57	74.86 ± 42.34
Current (*n* = 57)	7.23 ± 4.12	63.56 ± 11.47	10.31 ± 10.09	18.9 ± 7.39	74.93 ± 41.93
p Value	.6418	.3849	.3112	.8631	.9373

Notes. BMI = body mass index; PASE = Physical Activity Scale for the Elderly; REM = rapid eye movement. *p* Value from analysis of variance. Bold values indicate $p < .05$.

Table 2. Adjusted Means (95% Confidence Interval) of Sleep Staging Parameters by Mental Health Status

	Neither depressive nor anxiety symptoms (DEP–/ANX–)	*p* Value	Depressive symptoms only (DEP+)	*p* Value	Anxiety symptoms only (ANX+)	*p* Value	Both depressive and anxiety symptoms (DEP+/ANX+)	*p* Value
Sleep measures (%)								
% time Stage 1								
Model 1	6.81 (6.65, 6.98)	Reference	6.26 (5.40, 7.13)	.2219	6.93 (6.27, 7.58)	.7426	7.29 (6.40, 8.18)	.2974
Model 2	6.82 (6.65, 6.98)	Reference	6.10 (5.23, 6.97)	.2219	6.97 (6.32, 7.63)	.6549	7.28 (6.36, 8.20)	.3389
Model 3	6.81 (6.65, 6.97)	Reference	6.10 (5.26, 6.93)	.1008	6.91 (6.28, 7.54)	.7629	7.18 (6.30, 8.07)	.423
% time Stage 2								
Model 1	62.47 (62.10, 62.85)	Reference	**65.42 (63.49, 67.36)**	**.003**	63.00 (61.54, 64.46)	.4932	63.75 (61.76, 65.74)	.2164
Model 2	62.56 (62.19, 62.93)	Reference	**65.08 (63.15, 67.01)**	**.012**	62.36 (60.90, 63.82)	.7945	62.07 (60.02, 64.12)	.6483
Model 3	62.57 (62.19, 62.94)	Reference	**65.00 (63.07, 66.93)**	**.015**	62.26 (60.81, 63.71)	.6905	62.06 (60.03, 64.10)	.635
% time SWS								
Model 1	11.28 (10.93, 11.63)	Reference	11.28 (9.46, 13.09)	.9977	10.78 (9.41, 12.15)	.4904	11.44 (9.57, 13.31)	.8674
Model 2	11.26 (10.91, 11.61)	Reference	11.09 (9.26, 12.92)	.8574	11.09 (9.71, 12.47)	.8171	12.30 (10.36, 14.24)	.304
Model 3	11.25 (10.90, 11.60)	Reference	11.28 (9.46, 13.11)	.9746	11.00 (9.62, 12.38)	.729	12.42 (10.49, 14.34)	.2467
% time REM								
Model 1	19.44 (19.18, 19.69)	Reference	**17.05 (15.72, 18.37)**	**.0005**	19.30 (18.3, 20.30)	.7908	**17.52 (16.16, 18.88)**	**.007**
Model 2	19.36 (19.11, 19.62)	Reference	**17.73 (16.42, 19.05)**	**.018**	19.58 (18.58, 20.57)	.6811	18.35 (16.95, 19.75)	.1652
Model 3	19.37 (19.12, 19.62)	Reference	**17.63 (16.32, 18.93)**	**.0102**	19.83 (18.85, 20.81)	.3768	18.34 (16.96, 19.71)	.1496
REM latency (min)								
Model 1	73.13 (71.44, 74.83)	Reference	**87.34 (78.59, 96.09)**	**.0018**	**81.07 (74.47, 87.67)**	**.023**	**91.13 (82.15, 100.12)**	**.0001**
Model 2	74.31 (72.66, 75.95)	Reference	81.86 (73.35, 90.38)	.0886	75.35 (68.92, 81.78)	.7593	74.28 (65.25, 83.31)	.9956
Model 3	74.21 (72.57, 75.85)	Reference	81.40 (72.87, 89.93)	.1059	75.09 (68.67, 81.53)	.7942	73.51 (64.51, 82.52)	.8817

Notes. REM = rapid eye movement; SWS = slow wave sleep. Model 1: unadjusted. Model 2: adjusted for age, clinic, body mass index, race/ethnicity, education, physical activity, alcohol use, smoking status, cognitive impairment, hypertension, diabetes mellitus, rheumatoid arthritis, osteoarthritis, Parkinson's disease, myocardial infarction, congestive heart failure, chronic obstructive pulmonary disease, stroke, antidepressant use, benzodiazepine use, sleep medication use. Model 3: Model 2 + sleep efficiency, sleep duration, sleep latency, apnea–hypopnea index, and percent of sleep time with $SaO_2 < 90\%$.

All *p* values compared with the reference category, DEP–/ANX–. Bold values indicate $p < .05$.

depressive symptoms did not alter our observation that DEP+ men had a lower percentage of sleep time in REM.

We had no information on the duration of mood disturbances. Because prior research demonstrates differences in sleep architecture coinciding with episode duration (Dew et al., 1996), duration of depressive illness might explain this discrepancy between clinical and community settings. We relied solely on depressive symptom count and do not have full diagnostic measures (including the duration criteria required for an MDD diagnosis). Nevertheless, depressive symptoms are important in its own right because they are common among older adults (Blazer, 2003) and contribute to poor physical health (Achat et al., 2000), disability Whiteford et al., 2013; Chen et al., 2012, and reduced quality of life (Unützer et al., 2000).

Our results show associations between depressed mood and sleep architecture (increases in the percentages of Stage 2 and decreases in the percentage of REM sleep) that parallel changes occurring across age groups (see Table 1). Redline and colleagues (2004), comparing participants 37–54 years of age compared with 70+, noted a 5.1% increase in the percentage of time spent in Stage 2 sleep and a 1.7% decrease in the percentage of time spent in REM sleep. Comparing these age-related differences in sleep architecture with our adjusted findings in men with depressed mood (2.43% more spent in Stage 2 and 1.74% less spent in REM sleep) gives context to assess the magnitude of these effects and indicates that depressed mood may be associated with an acceleration of age-related changes to sleep.

Our finding that men with depressed mood spend more time in Stage 2 sleep suggests that men with depressed mood spend more time in lighter sleep. The implications of our finding that men with depressed mood spend less time in REM sleep are less direct but can be contextualized in view of previously documented associations of REM sleep with health outcomes. For example, increased mortality has been associated with both extreme high and low percentages of REM sleep (Dew et al., 2003). Declines in REM sleep have also been related to brain dysfunction in the elderly (Prinz et al., 1982), and patients diagnosed with probable Alzheimer's disease show decreased REM sleep expression compared with age-matched healthy controls (Reynolds et al., 1985). In rats, REM sleep deprivation contributes to a reduction in hippocampal neurogenesis (Guzman-Marin et al., 2008).

Although our study did not assess structural changes in the brain, the association between depressed mood and sleep architecture may reflect neurodegeneration. The "vascular hypothesis" of late-life depression suggests a distinct subtype of MDD in older adults characterized by cerebral hyperintensities (Taylor, Aizenstein, & Alexopoulos, 2013). Indeed, greater levels of vascular abnormalities in the brain have been related to faster aging-related health decline (Rosano et al., 2005). Because SDB may lead to vascular abnormalities in the brain and altered sleep architecture, we conducted a sensitivity analysis excluding participants with severe SDB. This analysis did not reproduce the finding of an independent association between depressed mood and more Stage 2 sleep, indicating that the relationship between depressed mood and greater levels of Stage 2 sleep may be driven in part by the increased rates of SDB found among men with mood disturbance. However, in this sensitivity analysis, depressed mood was still independently associated with less REM sleep. Future work including measures of brain structure should clarify whether neurodegeneration precedes or results from depressed mood and/or REM sleep architecture. Such future work can also investigate the roles of REM sleep and neurodegeneration in mediating the known association between depressed mood and risk of dementia (da Silva, Goncalves-Pereira, Xavier, & Mukaetova-Ladinska, 2013).

The strengths of our study include the novel examination of depression and anxiety symptoms separately in a large population-based sample of older men who were not selected on the basis of MH status or sleep disturbances. In addition, we adjusted for a wide array of medical, sleep, and lifestyle confounders. Our findings are robust and were consistent when excluding participants on relevant psychotropic medications, indicating that our findings are not a result of pharmacological treatment. These results were also similar when examining only individuals currently using antidepressant medication (used here as a proxy for diagnosis) or when examining a group of patients with more severe depressive symptoms using a higher GDS threshold. The differences in the percentage of time spent in Stage 2 and REM sleep were statistically significant albeit small and their clinical implications are unclear.

We acknowledge several limitations: We did not have true diagnostic measures of MDD and GAD limiting the comparison of the current study to previous clinical studies. Additionally, although the PSG measures were recorded in-home, which should afford participants more comfort than in a laboratory setting, only a single night of PSG recording was available and it is possible that "first-night" effects bias our results. But this "first-night" effect was not evident using in-home PSG in the Sleep Heart Health Study (Quan et al., 2002). Compared with a laboratory setting, in-home PSG lacks control over environmental conditions such as noise and light, and this may lead to bias in our results. Residual confounding by variables that we did not assess cannot be excluded. Our study was cross-sectional and we cannot comment on the temporal relations of sleep architecture and MH. Finally, our sample was 90.61% white men with an average age of 76.4; our results cannot be generalized to other ethnic groups, women, and younger men. Because age-related changes to REM sleep have not generally been observed after age 60 (Ohayon et al., 2004), future research across a broader age range is needed to examine potential interactive effects between age and depression in relation to sleep architecture.

In conclusion, in a large community-based sample of older men, depressed mood was associated with a lesser percentage of time spent in REM sleep. Our findings underscore the importance of examining community-based as well as clinical samples in seeking to understand the biology and health implications of mood disturbances. Future research is necessary to improve our understanding of the relationships between mood, sleep, brain, and overall health throughout the aging process.

Funding

The Osteoporotic Fractures in Men (MrOS) Study is supported by National Institutes of Health funding. The following institutes provide support: the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Institute on Aging, the National Center for Research Resources, and National Institutes of Health Roadmap for Medical Research under the following grant numbers: U01 AR45580, U01 AR45614, U01 AR45632, U01 AR45647, U01 AR45654, U01 AR45583, U01 AG18197, U01-AG027810, and UL1 RR024140. The National Heart, Lung, and Blood Institute provides funding for the MrOS Sleep ancillary study "Outcomes of Sleep Disorders in Older Men" under the following grant numbers: R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, R01 HL070837, R01 HL070838, and R01 HL070839. S. F. Smagula is supported by T32 AG000181.

References

Achat, H., Kawachi, I., Spiro, A., 3rd, DeMolles, D. A., & Sparrow, D. (2000). Optimism and depression as predictors of physical and mental health functioning: The Normative Aging Study. *Ann Behav Med*, 22, 127–130. doi:http://dx.doi.org/10.1007/BF02895776. PMID:10962705

Aikman, G., & Oehlert, M. (2001). Geriatric Depression Scale. *Clinical Gerontologist*, 22, 63–70. doi:10.1300/J018v22n03_07

Almeida, O. P., & Almeida, S. A. (1999). 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. *International Journal of Geriatric Psychiatry*, 14, 858–865. doi:10.1002/(SICI)1099-1166(199910)14:10<858::AID-GPS35>3.0.CO;2-8

Ancoli-Israel, S., Cole, R., Alessi, C., Chambers, M., Moorcroft, W., & Pollak, C. P. (2003). The role of actigraphy in the study of sleep and circadian rhythms. *Sleep*, 26, 342–392. PMID:12749557

Berry, R. B., Budhiraja, R., Gottlieb, D. J., Gozal, D., Iber, C., Kapur, V. K., … Tangredi, M. M. (2012). Rules for scoring respiratory events in sleep: Update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *Journal of Clinical Sleep Medicine*, 8, 597–619. doi:10.5664/jcsm.2172

Blackwell, T., Ancoli-Israel, S., Redline, S., Stone, K. L., & Osteoporotic Fractures in Men Study Group. (2011). Factors that may influence the classification of sleep-wake by wrist actigraphy: The MrOS Sleep Study. *Journal of Clinical Sleep Medicine*, 7, 357–367. doi:10.5664/JCSM.1190

Blackwell, T., Yaffe, K., Ancoli-Israel, S., Redline, S., Ensrud, K. E., Stefanick, M. L., & Stone, K. L. (2011). Associations between sleep architecture and sleep-disordered breathing and cognition in older community-dwelling men: The Osteoporotic Fractures in Men Sleep Study. *Journal of the American Geriatrics Society*, 59, 2217–2225. doi:10.1111/j.1532-5415.2011.03731.x

Blank, J. B., Cawthon, P. M., Carrion-Petersen, M. L., Harper, L., Johnson, J. P., Mitson, E., & Delay, R. R. (2005). Overview of recruitment for the osteoporotic fractures in men study (MrOS). *Contemporary Clinical Trials*, 26, 557–568. doi:10.1016/j.cct.2005.05.005

Blazer, D. G. (2003). Depression in late life: Review and commentary. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, 58, 249–265. doi:10.1093/gerona/58.3.M249, PMID:12634292

Chen, C. M., Mullan, J., Su, Y. Y., Griffiths, D., Kreis, I. A., & Chiu, H. C. (2012). The longitudinal relationship between depressive symptoms and disability for older adults: a population-based study. *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences*, 67, 1059–1067. doi:10.1093/gerona/gls074. http://dx.doi.org/10.1093/gerona/gls074

da Silva, J., Goncalves-Pereira, M., Xavier, M., & Mukaetova-Ladinska, E. B. (2013). Affective disorders and risk of developing dementia: Systematic review. *British Journal of Psychiatry*, 202, 177–186. doi:10.1192/bjp.bp.111.101931

Dew, M. A., Hoch, C. C., Buysse, D. J., Monk, T. H., Begley, A. E., Houck, P. R., & Reynolds, C. F., III. (2003). Healthy older adults' sleep predicts all-cause mortality at 4 to 19 years of follow-up. *Psychosomatic Medicine*, 65, 63–73. doi:10.1097/01.PSY.0000039756.23250.7C, PMID:12554816

Dew, M. A., Reynolds, C. F., III, Buysse, D. J., Houck, P. R., Hoch, C. C., Monk, T. H., & Kupfer, D. J. (1996). Electroencephalographic sleep profiles during depression. Effects of episode duration and other clinical and psychosocial factors in older adults. *Archives of General Psychiatry*, 53, 148–156. doi:10.1001/archpsyc.1996.01830020066008, PMID:8629890

Fuller, K. H., Waters, W. F., Binks, P. G., & Anderson, T. (1997). Generalized anxiety and sleep architecture: A polysomnographic investigation. *Sleep*, 20, 370–376. PMID:9381061

Gillin, J. C., Duncan, W. C., Murphy, D. L., Post, R. M., Wehr, T. A., Goodwin, F. K., & Bunney, W. E., Jr. (1981). Age-related changes in sleep in depressed and normal subjects. *Psychiatric Research*, 4, 73–78. doi:10.1016/0165-1781(81)90010-X

Goldberg, D., Bridges, K., Duncan-Jones, P., & Grayson, D. (1988). Detecting anxiety and depression in general medical settings. *British Medical Journal*, 297, 897–899. doi:10.1136/bmj.297.6653.897, PMID:3140969, PMCID:PMC1834427

Guzman-Marin, R., Suntsova, N., Bashir, T., Nienhuis, R., Szymusiak, R., & McGinty, D. (2008). Rapid eye movement sleep deprivation contributes to reduction of neurogenesis in the hippocampal dentate gyrus of the adult rat. *Sleep*, 31, 167–175. PMID:18274263, PMCID:PMC2225569

Knowles, J. B., & MacLean, A. W. (1990). Age-related changes in sleep in depressed and healthy subjects. A meta-analysis. *Neuropsychopharmacology*, 3, 251–259. PMID:2144733

Kostka, T., & Jachimowicz, V. (2010). Relationship of quality of life to dispositional optimism, health locus of control and self-efficacy in older subjects living in different environments. *Quality of Life Research*, 19, 351–361. doi:10.1007/s11136-010-9601-0

Kupfer, D. J., & Foster, F. G. (1972). Interval between onset of sleep and rapid-eye-movement sleep as an indicator of depression. *Lancet*, 2, 684–686. doi:10.1016/S0140-6736(72)92090-9

Lee, J. H., Reynolds, C. F., III, Hoch, C. C., Buysse, D. J., Mazumdar, S., George, C. J., & Kupfer, D. J. (1993). Electroencephalographic sleep in recently remitted, elderly depressed patients in double-blind placebo-maintenance therapy. *Neuropsychopharmacology*, 8, 143–150. doi:10.1038/npp.1993.16, PMID:8471126

Marc, L. G., Raue, P. J., & Bruce, M. L. (2008). Screening performance of the 15-item geriatric depression scale in a diverse elderly home care population. *American Journal of Geriatric Psychiatry*, 16, 914–921. doi:10.1097/JGP.0b013e318186bd67

Monti, J. M., & Monti, D. (2000). Sleep disturbance in generalized anxiety disorder and its treatment. *Sleep Medicine Reviews*, 4, 263–276. doi:10.1053/smrv.1999.0096

Morris, J. N. (1957). *Uses of epidemiology*. London: Churchill Livingstone.

Ohayon, M. M., Carskadon, M. A., Guilleminault, C., & Vitiello, M. V. (2004). Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: Developing normative sleep values across the human lifespan. *Sleep*, 27, 1255–1273. PMID:15586779

Orwoll, E., Blank, J. B., Barrett-Connor, E., Cauley, J., Cummings, S., Ensrud, K., & Stone, K. (2005). Design and baseline characteristics of the osteoporotic fractures in men (MrOS) study--a large observational study of the determinants of fracture in older men. *Contemporary Clinical Trials*, 26, 569–585. doi:10.1016/j.cct.2005.05.006

Pahor, M., Chrischilles, E. A., Guralnik, J. M., Brown, S. L., Wallace, R. B., & Carbonin, P. (1994). Drug data coding and analysis in epidemiologic studies. *European Journal of Epidemiology*, 10, 405–411. doi:10.1007/BF01719664, PMID:7843344

Papadimitriou, G. N., & Linkowski, P. (2005). Sleep disturbance in anxiety disorders. *International Review of Psychiatry*, 17, 229–236. doi:10.1080/09540260500104524

Paudel, M. L., Taylor, B. C., Diem, S. J., Stone, K. L., Ancoli-Israel, S., Redline, S., & Osteoporotic Fractures in Men Study Group. (2008). Association between depressive symptoms and sleep disturbances in community-dwelling older men. *Journal of the American Geriatrics Society*, 56, 1228–1235. doi:10.1111/j.1532-5415.2008.01753.x

Peterson, M. J., & Benca, R. M. (2011). Mood disorders. In M. H. Kryger, T. Roth, & W. C. Dement (Eds.), *Principles and practice of sleep medicine* (Vol. 5, pp. 1488–1500). Saint Louis, MO: Elsevier. doi:10.1016/B978-1-4160-6645-3.00130-4

Prinz, P. N., Peskind, E. R., Vitaliano, P. P., Raskind, M. A., Eisdorfer, C., Zemcuznikov, N., & Gerber, C. J. (1982). Changes in the sleep and waking EEGs of nondemented and demented elderly subjects. *Journal of the American Geriatrics Society*, 30, 86–93. PMID:7199061

Quan, S. F., Griswold, M. E., Iber, C., Nieto, F. J., Rapoport, D. M., Redline, S., & Young, T. (2002). Short-term variability of respiration and sleep during unattended nonlaboratory polysomnography--the Sleep Heart Health Study. [corrected]. *Sleep*, 25, 843–849. PMID:12489889

Rao, M. N., Blackwell, T., Redline, S., Stefanick, M. L., Ancoli-Israel, S., & Stone, K. L. (2009). Association between sleep architecture and measures of body composition. *Sleep*, 32, 483–490. PMID:19413142, PMCID:PMC2663862

Rechtschaffen, A., & Kales, A. (Eds.). (1968). *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects [NIH Publication 204]*. Washington, DC: National Institutes of Health.

Redline, S., Kirchner, H. L., Quan, S. F., Gottlieb, D. J., Kapur, V., & Newman, A. (2004). The effects of age, sex, ethnicity, and sleep-disordered breathing on sleep architecture. *Archives of Internal Medicine*, 164, 406–418. doi:10.1001/archinte.164.4.406

Redline, S., Sanders, M. H., Lind, B. K., Quan, S. F., Iber, C., Gottlieb, D. J., & Kiley, J. P. (1998). Methods for obtaining and analyzing unattended polysomnography data for a multicenter study. Sleep Heart Health Research Group. *Sleep*, 21, 759–767. PMID:11300121

Reynolds, C. F., III Frank, E., Hoch, C. C., Buysse, D. J., George, C. J., Houck, . . . Rifai, H. (1991). Sleep in late-life recurrent depression. Changes during early continuation therapy with nortriptyline. *Neuropsychopharmacology*, 5, 85–96. PMID:1930617

Reynolds, C. F., III, Kupfer, D. J., Taska, L. S., Hoch, C. C., Spiker, D. G., Sewitch, D. E., . . . Morycz, R. (1985). EEG sleep in elderly depressed, demented, and healthy subjects. *Biological Psychiatry*, 20, 431–442. doi:10.1016/0006-3223(85)90045-9

Rosano, C., Kuller, L. H., Chung, H., Arnold, A. M., Longstreth, W. T., Jr., & Newman, A. B. (2005). Subclinical brain magnetic resonance imaging abnormalities predict physical functional decline in high-functioning older adults. *Journal of the American Geriatrics Society*, 53, 649–654. doi:10.1111/j.1532-5415.2005.53214.x

Sheikh, J. I., & Yesavage, J. A. (1986). Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. *Clinical Gerontology*, 5, 165–173. doi:10.1300/J018v05n01_09

Taylor, W. D., Aizenstein, H. J., & Alexopoulos, G. S. (2013). The vascular depression hypothesis: Mechanisms linking vascular disease with depression. *Molecular Psychiatry*, 18, 963–974. doi:10.1038/mp.2013.20

Teng, E. L., & Chui, H. C. (1987). The Modified Mini-Mental State (3MS) examination. *Journal of Clinical Psychiatry*, 48, 314–318. PMID:3611032

Unützer, J., Patrick, D. L., Diehr, P., Simon, G., Grembowski, D., & Katon, W. (2000). Quality adjusted life years in older adults with depressive symptoms and chronic medical disorders. *International Psychogeriatrics,* 12, 15–33. http://dx.doi.org/10.1017/S1041610200006177. PMID:10798451

Vitiello, M. V., Prinz, P. N., Avery, D. H., Williams, D. E., Ries, R. K., Bokan, J. A., & Khan, A. (1990). Sleep is undisturbed in elderly, depressed individuals who have not sought health care. *Biological Psychiatry*, 27, 431–440. doi:10.1016/0006-3223(90)90553-E

Washburn, R. A., Smith, K. W., Jette, A. M., & Janney, C. A. (1993). The Physical Activity Scale for the Elderly (PASE): Development and evaluation. *Journal of Clinical Epidemiology*, 46, 153–162. doi:10.1016/0895-4356(93)90053-4

Whiteford, H. A., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E., . . . Vos, T. (2013). Global burden of disease attributable to mental and substance use disorders: Findings from the Global Burden of Disease Study 2010. *Lancet*, 382, 1575–1586. doi: 10.1016/s0140-6736(13)61611-6

Yesavage, J. A., Brink, T. L., Rose, T. L., Lum, O., Huang, V., Adey, M., & Leirer, V. O. (1982). Development and validation of a geriatric depression screening scale: A preliminary report. *Journal of Psychiatric Research*, 17, 37–49. doi:10.1016/0022-3956(82)90033-4