# UCLA UCLA Previously Published Works

## Title

Associations of objective versus subjective social isolation with sleep disturbance, depression, and fatigue in community-dwelling older adults.

## Permalink

https://escholarship.org/uc/item/9pq3k5dx

**Journal** Aging & mental health, 23(9)

**ISSN** 1360-7863

## **Authors**

Cho, Joshua Hyong-Jin Olmstead, Richard Choi, Hanbyul <u>et al.</u>

**Publication Date** 

2019-09-01

## DOI

10.1080/13607863.2018.1481928

Peer reviewed



# **HHS Public Access**

Aging Ment Health. Author manuscript; available in PMC 2020 September 01.

Published in final edited form as:

Author manuscript

Aging Ment Health. 2019 September; 23(9): 1130–1138. doi:10.1080/13607863.2018.1481928.

## Associations of Objective Versus Subjective Social Isolation with Sleep Disturbance, Depression, and Fatigue in Community-Dwelling Older Adults

Joshua Hyong-Jin Cho, MD, PhD<sup>1</sup>, Richard Olmstead, PhD<sup>1</sup>, Hanbyul Choi, MD<sup>2</sup>, Carmen Carrillo, MA, MHS<sup>3</sup>, Teresa E. Seeman, PhD<sup>3</sup>, and Michael R. Irwin, MD<sup>1</sup>

<sup>1</sup>·Cousins Center for Psychoneuroimmunology, Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, University of California, Los Angeles

<sup>2</sup> Department of Surgery, Stony Brook University School of Medicine

<sup>3</sup> Division of Geriatrics, David Geffen School of Medicine, University of California, Los Angeles

## Abstract

**Objective:** Older adults are at higher risk of experiencing social isolation, which has been linked to impaired physical and mental health. The link between social isolation and health might be due to objective deprivation of social network and/or subjective experience of loneliness. This community-based cross-sectional study examined whether the associations between social isolation and behavioral symptoms including sleep disturbance, depression, and fatigue are mostly explained by its subjective component.

**Methods:** Randomly selected 2541 community-dwelling individuals in Los Angeles aged 60 years were telephone-interviewed regarding their objective and subjective social isolation (respectively social network size and loneliness), sleep disturbance, depression, and fatigue.

**Results:** When objective and subjective social isolation were separately included in multivariate regression models, both were significantly associated with behavioral symptoms. However, once they were simultaneously included in the same multivariate models, while subjective social isolation remained strongly associated (adjusted beta 0.24 for sleep disturbance [P<0.001], 0.44 for depression [P<0.001], 0.17 for fatigue [P<0.001]), objective social isolation was weakly or non-significantly associated (-0.04 for sleep disturbance [P=0.03], -0.01 for depression [P=0.48], -0.003 for fatigue [P=0.89]). Additionally, those with objective social isolation were found to have worse symptoms mostly when they also experienced subjective social isolation.

**Conclusions:** Older adults with objective social isolation may experience sleep disturbance, depression, and fatigue because they feel socially isolated, not just because they are deprived of social networks. Interventions that target social isolation might serve as potential treatments for improving behavioral health of older adults, especially by targeting its subjective component.

Corresponding author: Dr. Cho, hjcho@mednet.ucla.edu. Declaration of Conflicting Interests None.

#### Keywords

social isolation; sleep disturbance; depression; fatigue; older adults

#### INTRODUCTION

Older adults are at higher risk of experiencing social isolation; they are more likely to report reduced social contact due to a loss of personal role in society, decreases in social network ties, barriers to access (e.g., mobility problems), a decreased ability to engage in reciprocal social relationships (e.g., increased frailty), and loneliness (Antonucci & Akiyama, 1987; Bisconti & Bergeman, 1999; Victor & Yang, 2012). In turn, social isolation in aging has been linked to not only impaired physical and mental health but also mortality (Holt-Lunstad, Smith, & Layton, 2010; Seeman, 2000). The link between social isolation and health might be due to objective deprivation of social network ties or subjective experience of social isolation. While objective social isolation has been described as "lack of contact with others due to situational factor, such as small size of social network, infrequent social interaction, or lack of participation in social activity", subjective social isolation has been characterized as "perceived shortage in one's social resources, such as companionship or social support" (Cornwell & Waite, 2009).

Older adults with reduced social network ties may not necessarily feel socially isolated, and thus objective and subjective social isolation may not necessarily co-exist. Indeed, the two variables have not been highly correlated with each other and may be distinct constructs (Coyle & Dugan, 2012; Perissinotto, Stijacic Cenzer, & Covinsky, 2012; Routasalo, Savikko, Tilvis, Strandberg, & Pitkala, 2006). Distinguishing between objective and subjective social isolation regarding their associations with health is important because understanding their relative contribution to health may shed light into their independent or dependent mechanisms and provide information on potential interventions (Holt-Lunstad, Smith, Baker, Harris, & Stephenson, 2015).

Objective social isolation has been consistently associated with physical and mental health and all-cause mortality—see Seeman (Seeman, 1996) and Nicholson (Nicholson, 2012) for reviews. Likewise, it also seems that subjective social isolation is associated with physical and mental health as well as mortality, although the existing evidence is more limited—see Hawkley and Cacioppo (Hawkley & Cacioppo, 2010) and Seeman (Seeman, 1996) for reviews. A few studies have concurrently examined objective and subjective social isolation (Golden et al., 2009; Holwerda et al., 2012; Houtjes et al., 2014; Penninx et al., 1999; Routasalo et al., 2006; Steptoe, Shankar, Demakakos, & Wardle, 2013; Tomaka, Thompson, & Palacios, 2006). However, the available evidence is mixed, with one study reporting that subjective social isolation had stronger effects on mortality than objective social isolation (Holwerda et al., 2012), whereas the other found that objective social isolation was more influential (Steptoe et al., 2013). A recent meta-analysis concluded that there is currently insufficient empirical evidence to distinguish the effects of objective and subjective social isolation on mortality (Holt-Lunstad et al., 2015).

In the current study, we focused on behavioral health outcomes such as sleep disturbance, depression, and fatigue, as these symptoms are highly prevalent among older adults and have been reported to impair functioning, quality of life, and physical health (Barua, Ghosh, Kar, & Basilio, 2011; Hardy & Studenski, 2010; Kamel & Gammack, 2006). Furthermore, while these behavioral symptoms are separate constructs and may occur independently, they are intimately related to one another. For example, sleep disturbance and fatigue are common symptoms of and also risk factors for depression (Cho et al., 2008; Mattisson et al., 2009); daytime fatigue is an obvious consequence of insomnia (Gradisar et al., 2007). Social isolation has been positively correlated with sleep disturbance, depression, and fatigue. It is thought that social isolation is associated with sleep disturbance through a disruption of social zeitgebers (i.e., social cues that maintain the sleep-wake activity schedule), which are increasingly viewed as being critical in the homeostatic regulation of sleep-wake activity (Mistlberger & Skene, 2004). Social isolation may serve as a stressor that produces negative affect (e.g., anxiety, depression), negative reactivity (e.g., irritability, hostility, mistrust), and lowered feelings of self-worth (Cacioppo & Hawkley, 2003). Both size and quality of social networks were associated with depressive symptoms in older adults (Litwin, Stoeckel, & Schwartz, 2015). Both social network and social support-i.e., emotional support, informational support, tangible support, positive social interaction, and affectionate support -were associated with lower levels of fatigue in Hodgkin lymphoma survivors (Soares et al., 2013). Breast cancer survivors who felt lonelier had more pain, depression, and fatigue (Jaremka et al., 2014). Socially isolated individuals-either subjectively or objectivelyreported poorer sleep quality and had poorer sleep efficiency compared to those who were not socially isolated (Cacioppo, Hawkley, Berntson, et al., 2002; Cacioppo, Hawkley, Crawford, et al., 2002; Eshkoor, Hamid, Nudin, & Mun, 2014; Friedman et al., 2005; Sinokki et al., 2010).

Our previous review—systematic but non-meta-analytic—found limited research that has concurrently evaluated these two types of social isolation and their associations with these behavioral symptoms, although limited evidence suggests a stronger association between subjective social isolation and symptoms of sleep disturbance and depression in older adults (Choi, Irwin, & Cho, 2015). Included in this review were the following studies examining the contribution of subjective and objective social isolation to behavioral symptoms simultaneously among older adults. In a prospective study focusing on sleep quality conducted in Dublin, Ireland, with a convenience sample of patients attending a clinic (N=447), subjective social isolation predicted poor sleep quality, but objective social isolation did not (McHugh & Lawlor, 2013). A cross-sectional study conducted in a Malaysian agricultural settlement (N=161) showed a stronger association between subjective social isolation and depression compared to that between objective social isolation and depression (Azam et al., 2013). A community-based study in Dublin assessed loneliness and social network concurrently and their associations with mood and wellbeing (N=1299), and again showed a stronger association of loneliness with depression compared to social network (Golden et al., 2009). On the other hand, a recent prospective study conducted in Taiwan (N=639) found a significant association between objective social isolation and poor sleep quality, whereas loneliness was not significantly associated with sleep quality (Yu, Steptoe, Niu, Ku, & Chen, 2018). Thus, most of the existing studies support a relatively

stronger association of subjective social isolation with sleep disturbance and depression, but an opposite pattern of findings has been reported as well.

The current study aimed to examine: 1) whether subjective social isolation is crosssectionally associated with behavioral symptoms including sleep disturbance, depression, and fatigue among community-dwelling older adults; 2) whether objective social isolation is associated with such symptoms; and 3) whether the association between social isolation and such symptoms is mostly explained by its subjective component. We operationally defined subjective social isolation as loneliness. Objective social isolation was defined as reduced social network size using the reported number of close friends and relatives. We hypothesized that: 1) Older adults who feel socially isolated are more likely to experience sleep disturbance, depression, and fatigue; 2) Those who have small social networks are more likely to experience sleep disturbance, depression, and fatigue; 3) The association of subjective social isolation with these symptoms is relatively more significant compared to objective social isolation.

#### METHODS

#### **Participants**

The population of interest for this cross-sectional study was community-dwelling individuals aged 60 years or older in Los Angeles, CA. The study received oversight and approval from the University of California Los Angeles Institutional Review Board (IRB#11-000656). Given our focus on older adults, a telephone survey using age-targeted sampling methods was conducted over 2 years in 2010 and 2011. This targeted approach has been shown far more cost-effective than random digit dialing methods (Psaty et al., 1991). Lists of telephone numbers and mailing addresses of households with at least one person aged 60 years or older in Los Angeles, CA, were purchased from GENESYS Sampling Systems (Fort Washington, PA), a company that maintains a bimonthly updated database of all available listed telephone households in the US. Age information for each household was based on either known agerelated data or a statistical estimate of age, predicted on individual household characteristics and Census demographic information. The actual age information was available for 95.9% of the households that had at least one person aged 60 years or older, whereas statistically inferred age was available for the remainder. Various national and regional surveys have used the GENESYS database for both random-digit-dial and targeted samplings (O'Malley & Forrest, 2002; Runyan et al., 2005). An advance letter was sent to 29,550 potential survey participants, informing them of the purpose of the study and a follow up telephone call. Individuals who did not return the refusal card within 2 weeks were contacted by telephone to obtain oral consent for a telephone interview. Trained interviewers conducted the survey using a computer-assisted telephone interview (CATI) methodology. A total of 2963 individuals were surveyed, thus 10.0% of all contacted individuals. These 2963 individuals provided verbal informed consent. We excluded 422 individuals with missing values on any of the independent, dependent, or confounding variables from the current analyses. Compared to the final analytic sample (N=2541), excluded individuals were less educated: although the actual difference was small (mean education 15.5 years vs. 15.3 years), it was statistically significant due to the large sample size (t=2.46, P=0.01). Excluded individuals

were also more likely to be retired (64.0% vs. 72.6%,  $X^2$ =13.56, P=0.001). However, they were not significantly different regarding age, sex, ethnicity, marital status, body-mass index (BMI), medical comorbidity, alcohol consumption, smoking, physical activity level, loneliness, social network size, sleep quality, depressive symptoms, or fatigue (P's>0.05).

#### Independent Variables: Objective and Subjective Social Isolation

Social network size was assessed as an objective measure of social isolation. Social network size reflects the mean of reported number of close friends and of close relatives (Seeman, Gruenewald, Cohen, Williams, & Matthews, 2014). As available answer categories for the numbers of close friends and of close relatives were intervals (0, 1-2, 3-5, 6-9, and 10+), midpoint values (respectively 0, 1.5, 4, 7.5, and 12) were assigned to each category and then summed up; thus social network size ranges from 0 to 24 and higher scores means larger social networks. Loneliness, as a measure of subjective social isolation, was assessed using a 4-item questionnaire, which has been adapted from Seeman and Syme (Seeman & Syme, 1987) and used in several phases of the Coronary Artery Risk Development in Young Adults (CARDIA) Study (Borrell et al., 2007; Cho, Seeman, Kiefe, Lauderdale, & Irwin, 2015). The 4 items include "feel lonely", "feel that other people really care for you", "find yourself wishing someone would comfort you", and "wish you had more close friends". Each item is on a four-point scale (0-3), and the total score, which ranges from 0 to 12, is calculated in such a way that higher scores reflect higher loneliness. Cronbach's alpha assessed for internal consistency was of 0.60. Social network size and loneliness were used as continuous variables in their original format for most statistical analyses. In additional analyses evaluating the findings in the clinical context, objective and subjective social isolation variables were dichotomized using median splits.

#### Dependent Variables: Sleep Disturbance, Depressive Symptoms, and Fatigue

The Pittsburgh Sleep Quality Index (PSQI) was used to assess perceived sleep disturbance evaluating components such as subjective sleep quality, sleep latency and use of sleep medications—during the past month (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Global total scores (range 0–20) were used as a continuous variable for most statistical analyses. The Center for Epidemiological Studies Depression Scale with 10 items (CES-D) was used to assess depressive symptoms (Irwin, Artin, & Oxman, 1999). Total scores (range 0–10) were used as a continuous variable for most analyses. Fatigue was assessed with the Chalder Fatigue Questionnaire (CFQ), an 11-item questionnaire widely used to measure physical and mental fatigue (Chalder et al., 1993). Total scores by likert scoring (range 0– 33) were used as a continuous variable for most analyses. In additional analyses evaluating the findings in the clinical context, sleep disturbance was dichotomized using the standard PSQI cutoff (>5) (Buysse et al., 1989), depression using the validated CES-D cutoff in older adults ( 4) (Irwin et al., 1999), and fatigue using the standard cutoff (bimodal score 4) (Chalder et al., 1993).

#### **Potential Confounding Variables**

Information on demographic variables including age, sex, ethnicity, education, marital status, and employment status was obtained. Education was used as a measure of socioeconomic status (Winkleby, Jatulis, Frank, & Fortmann, 1992). Biomedical and health-

related variables including weight and height (hence BMI), alcohol consumption in the past week, smoking, physical activity levels, and comorbid medical disorders using the Charlson Comorbidity Index (CCI) (Charlson, Pompei, Ales, & MacKenzie, 1987) were assessed.

Analysis

For the purpose of describing characteristics of 2541 participants, objective and subjective social isolation were dichotomized using median splits, respectively social network size 12 vs <12 and loneliness score <4 vs. 4. Their characteristics were described in terms of frequency or mean by levels of objective and subjective social isolation, using chi-square tests or t-tests. Then the study hypotheses were tested by performing multivariate linear regression analyses with standardized regression coefficients (beta), which facilitate comparison across models. Both the independent and dependent variables were used as continuous in their original formats. Selection of covariates for multivariate analyses relied on empirical evidence rather than predetermined P-value criteria. The latter approach, which selects factors for inclusion in a multivariate model only if the factors are 'statistically significant' in bivariate screening, is considered less optimal; a factor can be a confounder even if it is not statistically significant by itself because it changes the effect of the exposure of interest when it is included in the model, or because it is a confounder only when included with other covariates (Sun, Shook, & Kay, 1996). Thus, the following covariates were selected and included in all multivariate models: age, sex, ethnicity, education, marital status, employment status, BMI, medical comorbidity, smoking, alcohol consumption, and physical activity. The first hypothesis tested was whether subjective social isolation was associated with symptoms of sleep disturbance, depression, and fatigue; in which the independent variable was subjective social isolation; and the dependent variable was sleep disturbance, depressive symptoms, or fatigue. The second hypothesis, whether objective social isolation was associated with these behavioral symptoms, was tested using the same approach. To contextualize the findings for the clinical setting, the first and second hypotheses were also tested using multivariate logistic regression analyses with binary independent and dependent variables dichotomized based on clinical outpoints. The third hypothesis tested was whether the association of subjective social isolation with these behavioral symptoms was relatively more significant compared to objective social isolation. To test this hypothesis, both measures of objective and subjective social isolation were simultaneously included in the same multivariate linear regression models, in addition to the dependent variables and all the covariates. Then, the adjusted betas and the respective statistical significances were compared. Additionally, in order to assess the separate and combined contribution of objective and subjective social isolation to behavioral symptoms, providing further information on their relative contribution, a composite variable of these two measures was generated with 4 categories (low/low, high/low, low/high, and high/high) using the median splits. Given the large sample size, for the interpretation of the findings in terms of their magnitude, statistical significance as well as effect size was taken into consideration. Based on Cohen (Cohen, 1992), 0.10, 0.30, and 0.50 were considered respectively small, medium, and large for standardized regression coefficient (beta) and correlation coefficient (r). All analyses were performed using STATA 14.1 (StataCorp. College Station, TX).

## RESULTS

#### Sample Characteristics

The mean age of the final analytical sample (N=2541) was 72.6 years (standard deviation [SD] 8.4) and the age range was 60–103; 46.6% were females (Supplemental Table). Tables 1a and 1b describe participant characteristics according to the levels of subjective and objective social isolation. The following variables were significantly associated with subjective social isolation: younger age, being female, being non-partnered, being non-retired, lower alcoholic consumption, being a current smoker, lower physical activity, worse sleep quality, worse depressive symptoms, and worse fatigue. The following variables were significantly associated with objective social isolation: younger age, lower education, being non-partnered, lower alcoholic consumption, lower physical activity, worse sleep quality, worse depressive symptoms, and worse fatigue. Besides behavioral symptoms, meaningful differences beyond a statistical significance included younger age, non-partnered status, and lower physical activity of isolated participants (either subjectively or objectively).

#### Subjective Social Isolation and Behavioral Symptoms

**Main Analyses Using Continuous Variables:** In unadjusted analyses, subjective social isolation was associated with each of the behavioral symptoms (unadjusted beta: 0.27, P<0.001 for sleep disturbance; 0.48, P<0.001 for depression; and 0.19, P<0.001 for fatigue). Based on Cohen (Cohen, 1992), betas for sleep disturbance and depression were respectively "medium" and "large". As shown in Table 2, these associations remained statistically significant after adjusting for all covariates including sociodemographic characteristics, BMI, medical comorbidity, smoking, alcohol consumption, and physical activity (adjusted betas: 0.25, P<0.001 for sleep disturbance; 0.44, P<0.001 for depression; and 0.17, P<0.001 for fatigue).

Additional Analyses Using Dichotomized Variables: To interpret the findings in a clinical context expressing the magnitude of associations in odds ratios, dependent variables —i.e., sleep disturbance, depression, and fatigue—were dichotomized using the standard cutoff scores as described in the methods section. Objective and subjective social improvement variables were dichotomized using median splits. In multivariate logistic regression analyses adjusted for all the covariates, subjective social isolation was significantly associated with behavioral symptoms (adjusted odds ratio [OR] 1.9, 95% confidence interval [CI] 1.6–2.2, P<0.001 for sleep disturbance; 4.4, 3.4–5.7, P<0.001 for depression; and 2.0, 1.6–2.4, P<0.001 for fatigue).

#### **Objective Social Isolation and Behavioral Symptoms**

**Main Analyses Using Continuous Variables:** In unadjusted analyses, objective social isolation was associated with each of the behavioral symptoms (unadjusted beta: -0.12, P<0.001 for sleep disturbance; -0.15, P<0.001 for depression; and -0.06, P=0.003 for fatigue). Based on Cohen (Cohen, 1992), betas for sleep disturbance and fatigue were "small". As shown in Table 2, these associations remained statistically significant after adjusting for all the covariates (adjusted betas: -0.10, P<0.001 for sleep disturbance; -0.11, P<0.001 for depression; and -0.04, P=0.04 for fatigue).

Additional Analyses Using Dichotomized Variables: In multivariate logistic regression analyses adjusted for all the covariates, objective social isolation was significantly associated with sleep disturbance and depression (adjusted OR 1.3, 95% CI 1.1–1.5, P=0.002 for sleep disturbance; 1.5, 1.2–1.9, P=0.001 for depression; and 1.2, 1.0–1.5, P=0.06 for fatigue).

#### Relative Contribution of Objective vs. Subjective Social Isolation to Behavioral Symptoms

**Main Analyses Using Individual Social Isolation Variables:** The magnitude of the correlation between objective and subjective social isolation was medium (r = -0.25, P<0.001). Objective and subjective social isolation were separately independent risk factors for each of the behavioral symptoms as described above. However, once objective and subjective social isolation were simultaneously included in the same multivariate models, while subjective social isolation remained strongly associated with all of the behavioral symptoms (adjusted beta 0.24 for sleep disturbance [P<0.001], 0.44 for depression [P<0.001], 0.17 for fatigue [P<0.001]), objective social isolation was weakly or non-significantly associated (-0.04 for sleep disturbance [P=0.03], -0.01 for depression [P=0.48], -0.003 for fatigue [P=0.89]). In fact, the associations between subjective social isolation and behavioral symptoms were substantially attenuated (Table 2).

Additional Analyses Using Composite Social Isolation Variables: Additional analyses assessed the separate and combined contribution of categorically defined objective and subjective social isolation to behavioral symptoms, providing further information on the relative contribution of objective vs. subjective social isolation to behavioral symptoms. Having both objective and subjective social isolation at low levels ("low/low"), i.e., below the medians, was defined as the reference category. As shown in Table 3, having high objective and high subjective social isolation ("high/high") was robustly related to each of the behavioral symptoms (betas ranging from 0.12 to 0.31 with Ps<0.001). Similarly, having low objective yet high subjective social isolation ("low/high") was also strongly associated with behavioral symptoms (betas ranging from 0.10 to 0.19 with Ps<0.001). In contrast, having high objective and low subjective social isolation ("high/low") was non-significantly or weakly associated with behavioral symptoms (betas ranging from 0.10 to 0.19 with Ps<0.001). In contrast, having high objective and low subjective social isolation ("high/low") was non-significantly or weakly associated with behavioral symptoms (betas ranging from 0.10 to 0.19 with Ps<0.001). In contrast, having high objective and low subjective social isolation ("high/low") was non-significantly or weakly associated with behavioral symptoms (betas ranging from -0.004 to 0.06). In other words, the contribution of objective social isolation without subjective social isolation was negligible to small, whereas the contribution of subjective social isolation.

#### DISCUSSION

In this large sample of community-dwelling older adults, both objective and subjective social isolation were cross-sectionally associated with symptoms of sleep disturbance, depression, and fatigue. The associations between social isolation and these behavioral symptoms were of a medium to large magnitude for depression and of a small to medium magnitude for sleep disturbance and fatigue. Furthermore, these associations were independent of various potential confounders such as sociodemographic characteristics, BMI, medical comorbidity, smoking, alcohol consumption, and physical activity. Most

importantly, when both objective and subjective social isolation were simultaneously included in the analyses, the associations between objective social isolation and behavioral symptoms were substantially attenuated. On the other hand, the associations between subjective social isolation and behavioral symptoms remained strong and practically unchanged, suggesting that those between objective social isolation and behavioral symptoms may be mostly explained by subjective social isolation. Indeed, additional analyses revealed that the separate contribution of objective social isolation to behavioral symptoms was negligible, while the separate contribution of subjective social isolation was almost comparable to the combined contribution of both measures. Older adults with objective social isolation had worse sleep disturbance, depression, and fatigue mostly when they also experienced subjective social isolation. In summary, older adults who either had small social networks or felt lonely were more likely to be sleep disturbed, depressed, and fatigued. Moreover, older adults with objective social isolation appeared to experience these symptoms mostly when they also had the subjective feeling of social isolation, not just because they were simply deprived of social networks.

Given the cross-sectional nature of the current study, however, the associations between social isolation and behavioral symptoms could be bidirectional. Thus, it is also possible that depressed, insomniac, or tired individuals become socially isolated and also poorly rate the quality of their social relationships. Indeed, when we tested the models with sleep disturbance, depression, and fatigue as independent variables and social isolation variables as dependent variables, the results were similar (data not shown).

This study examined an important but poorly explored topic regarding the distinctive contribution of objective vs. subjective social isolation to behavioral symptoms among older adults using a large community sample. The current study extends the prior research—reviewed in the introduction—by using multivariate regression in a large community sample of older adults, and provides evidence on the relative contributions of objective vs. subjective social isolation to sleep, depression, and fatigue. Additionally, the magnitude of the correlation between objective and subjective social isolation was medium in this study, in accordance with the extant literature, which reports that the two variables are not highly correlated with each other and may be distinct constructs (Coyle & Dugan, 2012; Perissinotto et al., 2012; Routasalo et al., 2006).

Of note, the associations between social isolation and behavioral symptoms were strong. For example, adjusted OR for subjective social isolation and depression was almost 4. According to a meta-analysis of older adult prospective studies, the most important risk factors for depression including bereavement and sleep disturbance had smaller ORs (respectively pooled OR 3.3 and 2.6) (Cole & Dendukuri, 2003). Furthermore, according to a cross-sectional study of community-dwelling older adults using CES-D for depression assessment, hence more comparable to the current study, insomnia was an important risk factor for depression with a prevalence ratio 1.83 (Alcantara et al., 2016).

This community-based cross-sectional study overcomes the limitations of prior studies, given the following strengths. First, the large sample of older adults randomly selected from the community minimized selection bias and increased generalizability. While previous

studies included 447 (McHugh & Lawlor, 2013), 161 (Azam et al., 2013), 639 (Yu et al., 2018), and 1299 participants (Golden et al., 2009), the current study included 2541 participants. Second, the associations between social isolation and behavioral symptoms were independent of a series of confounding variables such as sociodemographic characteristics, obesity, medical comorbidity, and health-related behaviors. However, the following limitations should be considered. First, the cross-sectional design of this study did not allow any inference on the directionality of the associations between social isolation and behavioral symptoms. Second, the assessment of sleep disturbance, depression, and fatigue relied on self-report questionnaires in lieu of procedures such as polysomnography and structured diagnostic interviews. However, assessment of these problems in clinical practice primarily relies on patients' self-report. Third, although we carefully performed multivariate analyses considering a series of potential confounders, it is still possible that there is some residual confounding since this was not a randomized controlled trial, the only approach that can eliminate the confounding effect entirely. Fourth, out of 2963 respondents, 422 were excluded due to missing values, hence about 14%, which could have introduced a selection bias. However, an assuring aspect against the possibility of such a bias was that none of the characteristics were significantly different between the included and excluded respondents except for retirement status.

Prospective and intervention studies are needed to evaluate the temporal and causal links between social isolation and behavioral symptoms. In particular, future studies should test whether interventions that target social isolation might serve as potential treatments for improving behavioral health of older adults. Furthermore, the findings of this study suggest that interventions that target subjective social isolation, as opposed to objective social isolation, may demonstrate greater trial efficacy as measured by improvements in sleep disturbance, depression, and fatigue. Previous intervention efforts in reducing social isolation have mostly focused on the objective components, e.g., by promoting networking (Saito, Kai, & Takizawa, 2012) or socialization (Sheridan et al., 2015), and have had limited success (Findlay, 2003). Thus, interventions focusing on social cognition (Masi, Chen, Hawkley, & Cacioppo, 2011) or sense of social belonging (Walton & Cohen, 2011) may be more useful in improving behavioral health outcomes.

In conclusion, while social isolation—either subjective or objective—was associated with behavioral symptoms including sleep disturbance, depression, and fatigue, the association of social isolation with these symptoms appears to be mostly explained by its subjective component.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

#### Acknowledgments

#### Funding

This research was funded by National Institutes of Health R01AG034588, and in part by R01AG026364, R01CA160245, R01DA032922, R01HL095799, P30AG028748, R01CA119159; R01CA160245; the Cousins Center for Psychoneuroimmunology, and UCLA Claude D. Pepper Older Americans Independence Center (MRI).

Additionally, the first author (JHC) was supported by K23AG049085, NIH/NCATS UCLA CTSI Grant KL2TR000122, and NARSAD Young Investigator Grant (22329) from the Brain and Behavior Research Foundation, 22329.

### REFERENCES

- Alcantara C, Biggs ML, Davidson KW, Delaney JA, Jackson CL, Zee PC, ... Redline S (2016). Sleep Disturbances and Depression in the Multi-Ethnic Study of Atherosclerosis. Sleep, 39(4), 915–925. doi: 10.5665/sleep.5654 [PubMed: 26715223]
- Antonucci TC, & Akiyama H (1987). Social networks in adult life and a preliminary examination of the convoy model. J Gerontol, 42(5), 519–527 [PubMed: 3624811]
- Azam WM, Yunus WM, Din NC, Ahmad M, Ghazali SE, Ibrahim N, ... Razali R (2013). Loneliness and depression among the elderly in an agricultural settlement: Mediating effects of social support. Asia-Pacific Psychiatry, 5(S1), 134–139 [PubMed: 23857850]
- Barua A, Ghosh MK, Kar N, & Basilio MA (2011). Prevalence of depressive disorders in the elderly. Ann Saudi Med, 31(6), 620–624. doi: 10.4103/0256-4947.87100 [PubMed: 22048509]
- Bisconti TL, & Bergeman CS (1999). Perceived social control as a mediator of the relationships among social support, psychological well-being, and perceived health. Gerontologist, 39(1), 94–103 [PubMed: 10028775]
- Borrell LN, Jacobs DR Jr., Williams DR, Pletcher MJ, Houston TK, & Kiefe CI (2007). Self-reported racial discrimination and substance use in the Coronary Artery Risk Development in Adults Study. Am J Epidemiol, 166(9), 1068–1079 [PubMed: 17698506]
- Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, & Kupfer DJ (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res, 28(2), 193– 213 [PubMed: 2748771]
- Cacioppo JT, & Hawkley LC (2003). Social isolation and health, with an emphasis on underlying mechanisms. Perspect Biol Med, 46(3 Suppl), S39–52 [PubMed: 14563073]
- Cacioppo JT, Hawkley LC, Berntson GG, Ernst JM, Gibbs AC, Stickgold R, & Hobson JA (2002). Do lonely days invade the nights? Potential social modulation of sleep efficiency. Psychol Sci, 13(4), 384–387 [PubMed: 12137144]
- Cacioppo JT, Hawkley LC, Crawford LE, Ernst JM, Burleson MH, Kowalewski RB, ... Berntson GG (2002). Loneliness and health: potential mechanisms. Psychosom Med, 64(3), 407–417 [PubMed: 12021415]
- Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, & Wallace EP (1993). Development of a fatigue scale. J Psychosom Res, 37(2), 147–153 [PubMed: 8463991]
- Charlson ME, Pompei P, Ales KL, & MacKenzie CR (1987). A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. Journal of Chronic Diseases, 40(5), 373–383 [PubMed: 3558716]
- Cho HJ, Lavretsky H, Olmstead R, Levin MJ, Oxman MN, & Irwin MR (2008). Sleep disturbance and depression recurrence in community-dwelling older adults: a prospective study. Am J Psychiatry, 165(12), 1543–1550. doi: 10.1176/appi.ajp.2008.07121882 [PubMed: 18765482]
- Cho HJ, Seeman TE, Kiefe CI, Lauderdale DS, & Irwin MR (2015). Sleep disturbance and longitudinal risk of inflammation: Moderating influences of social integration and social isolation in the Coronary Artery Risk Development in Young Adults (CARDIA) study. Brain Behavior and Immunity, 46, 319–326. doi: 10.1016/j.bbi.2015.02.023
- Choi H, Irwin MR, & Cho HJ (2015). Impact of social isolation on behavioral health in elderly: Systematic review. World Journal of Psychiatry, 5(4), 432–438. doi: 10.5498/wjp.v5.i4.432 [PubMed: 26740935]
- Cohen J (1992). A power primer. Psychol Bull, 112(1), 155–159 [PubMed: 19565683]
- Cole MG, & Dendukuri N (2003). Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. Am J Psychiatry, 160(6), 1147–1156. doi: 10.1176/appi.ajp. 160.6.1147 [PubMed: 12777274]
- Cornwell EY, & Waite LJ (2009). Social disconnectedness, perceived isolation, and health among older adults. J Health Soc Behav, 50(1), 31–48 [PubMed: 19413133]

- Coyle CE, & Dugan E (2012). Social isolation, loneliness and health among older adults. J Aging Health, 24(8), 1346–1363. doi: 10.1177/0898264312460275 [PubMed: 23006425]
- Eshkoor SA, Hamid TA, Nudin SS a. H, & Mun CY (2014). Importance of Hypertension and Social Isolation in Causing Sleep Disruption in Dementia. American Journal of Alzheimer's Disease and Other Dementias, 29(1), 61–66. doi: 10.1177/1533317513505136
- Findlay RA (2003). Interventions to reduce social isolation amongst older people: where is the evidence? Ageing and Society, 23(05), 647–658
- Friedman EM, Hayney MS, Love GD, Urry HL, Rosenkranz MA, Davidson RJ, ... Ryff CD (2005). Social relationships, sleep quality, and interleukin-6 in aging women. Proc Natl Acad Sci U S A, 102(51), 18757–18762. doi: 10.1073/pnas.0509281102 [PubMed: 16339311]
- Golden J, Conroy RM, Bruce I, Denihan A, Greene E, Kirby M, & Lawlor BA (2009). Loneliness, social support networks, mood and wellbeing in community-dwelling elderly. Int J Geriatr Psychiatry, 24(7), 694–700. doi: 10.1002/gps.2181 [PubMed: 19274642]
- Gradisar M, Lack L, Richards H, Harris J, Gallasch J, Boundy M, & Johnston A (2007). The Flinders Fatigue Scale: Preliminary Psychometric Properties and Clinical Sensitivity of a New Scale for Measuring Daytime Fatigue associated with Insomnia. Journal of Clinical Sleep Medicine: JCSM: official publication of the American Academy of Sleep Medicine, 3(7), 722–728 [PubMed: 18198807]
- Hardy SE, & Studenski SA (2010). Qualities of fatigue and associated chronic conditions among older adults. J Pain Symptom Manage, 39(6), 1033–1042. doi: 10.1016/j.jpainsymman.2009.09.026 [PubMed: 20538185]
- Hawkley LC, & Cacioppo JT (2010). Loneliness matters: a theoretical and empirical review of consequences and mechanisms. Ann Behav Med, 40(2), 218–227. doi: 10.1007/ s12160-010-9210-8 [PubMed: 20652462]
- Holt-Lunstad J, Smith TB, Baker M, Harris T, & Stephenson D (2015). Loneliness and social isolation as risk factors for mortality: a meta-analytic review. Perspect Psychol Sci, 10(2), 227–237. doi: 10.1177/1745691614568352 [PubMed: 25910392]
- Holt-Lunstad J, Smith TB, & Layton JB (2010). Social relationships and mortality risk: a metaanalytic review. PLoS Med, 7(7), e1000316. doi: 10.1371/journal.pmed.1000316 [PubMed: 20668659]
- Holwerda TJ, Beekman AT, Deeg DJ, Stek ML, van Tilburg TG, Visser PJ, ... Schoevers RA (2012). Increased risk of mortality associated with social isolation in older men: only when feeling lonely? Results from the Amsterdam Study of the Elderly (AMSTEL). Psychol Med, 42(4), 843–853. doi: 10.1017/S0033291711001772 [PubMed: 21896239]
- Houtjes W, van Meijel B, van de Ven PM, Deeg D, van Tilburg T, & Beekman A (2014). The impact of an unfavorable depression course on network size and loneliness in older people: a longitudinal study in the community. Int J Geriatr Psychiatry, 29(10), 1010–1017. doi: 10.1002/gps.4091 [PubMed: 24615822]
- Irwin M, Artin KH, & Oxman MN (1999). Screening for depression in the older adult: criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). Archives of Internal Medicine, 159(15), 1701–1704 [PubMed: 10448771]
- Jaremka LM, Andridge RR, Fagundes CP, Alfano CM, Povoski SP, Lipari AM, ... Kiecolt-Glaser JK (2014). Pain, depression, and fatigue: loneliness as a longitudinal risk factor. Health Psychol, 33(9), 948–957. doi: 10.1037/a0034012 [PubMed: 23957903]
- Kamel NS, & Gammack JK (2006). Insomnia in the elderly: cause, approach, and treatment. Am J Med, 119(6), 463–469. doi: 10.1016/j.amjmed.2005.10.051 [PubMed: 16750956]
- Litwin H, Stoeckel KJ, & Schwartz E (2015). Social networks and mental health among older Europeans: are there age effects? Eur J Ageing, 12(4), 299–309. doi: 10.1007/s10433-015-0347-y [PubMed: 28804362]
- Masi CM, Chen HY, Hawkley LC, & Cacioppo JT (2011). A meta-analysis of interventions to reduce loneliness. Pers Soc Psychol Rev, 15(3), 219–266. doi: 10.1177/1088868310377394 [PubMed: 20716644]

- Mattisson C, Bogren M, Horstmann V, Tambs K, Munk-Jorgensen P, & Nettelbladt P (2009). Risk factors for depressive disorders in the Lundby cohort--a 50 year prospective clinical follow-up. J Affect Disord, 113(3), 203–215. doi: 10.1016/j.jad.2008.07.002 [PubMed: 18694601]
- McHugh JE, & Lawlor BA (2013). Perceived stress mediates the relationship between emotional loneliness and sleep quality over time in older adults. Br J Health Psychol, 18(3), 546–555. doi: 10.1111/j.2044-8287.2012.02101.x [PubMed: 22988915]
- Mistlberger RE, & Skene DJ (2004). Social influences on mammalian circadian rhythms: animal and human studies. Biol Rev Camb Philos Soc, 79(3), 533–556 [PubMed: 15366762]
- Nicholson NR (2012). A review of social isolation: an important but underassessed condition in older adults. J Prim Prev, 33(2–3), 137–152. doi: 10.1007/s10935-012-0271-2 [PubMed: 22766606]
- O'Malley AS, & Forrest CB (2002). Primary Care Performance and the Patient-physician Relationship for Low-income Women. J Gen Intern Med, 17(1), 66–74 [PubMed: 11903777]
- Penninx BW, van Tilburg T, Kriegsman DM, Boeke AJ, Deeg DJ, & van Eijk JT (1999). Social network, social support, and loneliness in older persons with different chronic diseases. J Aging Health, 11(2), 151–168 [PubMed: 10558434]
- Perissinotto CM, Stijacic Cenzer I, & Covinsky KE (2012). Loneliness in older persons: a predictor of functional decline and death. Arch Intern Med, 172(14), 1078–1083. doi: 10.1001/archinternmed. 2012.1993 [PubMed: 22710744]
- Psaty BM, Cheadle A, Curry S, McKenna T, Koepsell TD, Wickizer T, ... Wagner EH (1991). Sampling Elderly in the Community: A Comparison of Commercial Telemarketing Lists and Random Digit Dialing Techniques for Assessing Health Behaviors and Health Status. American Journal of Epidemiology, 134(1), 96–106 [PubMed: 1853865]
- Routasalo PE, Savikko N, Tilvis RS, Strandberg TE, & Pitkala KH (2006). Social contacts and their relationship to loneliness among aged people - A population-based study. Gerontology, 52(3), 181–187. doi: 10.1159/000091828 [PubMed: 16645299]
- Runyan CW, Johnson RM, Yang J, Waller AE, Perkis D, Marshall SW, ... McGee KS (2005). Risk and protective factors for fires, burns, and carbon monoxide poisoning in US households. American Journal of Preventive Medicine, 28(1), 102–108 [PubMed: 15626564]
- Saito T, Kai I, & Takizawa A (2012). Effects of a program to prevent social isolation on loneliness, depression, and subjective well-being of older adults: a randomized trial among older migrants in Japan. Arch Gerontol Geriatr, 55(3), 539–547. doi: 10.1016/j.archger.2012.04.002 [PubMed: 22564362]
- Seeman TE (1996). Social ties and health: the benefits of social integration. Annals of Epidemiology, 6(5), 442–451 [PubMed: 8915476]
- Seeman TE (2000). Health promoting effects of friends and family on health outcomes in older adults. American Journal of Health Promotion, 14(6), 362–370 [PubMed: 11067571]
- Seeman TE, Gruenewald TL, Cohen S, Williams DR, & Matthews KA (2014). Social relationships and their biological correlates: Coronary Artery Risk Development in Young Adults (CARDIA) study. Psychoneuroendocrinology, 43, 126–138. doi: 10.1016/j.psyneuen.2014.02.008 [PubMed: 24703178]
- Seeman TE, & Syme SL (1987). Social networks and coronary artery disease: a comparison of the structure and function of social relations as predictors of disease. Psychosomatic Medicine, 49(4), 341–354 [PubMed: 3615763]
- Sheridan AJ, Drennan J, Coughlan B, O'Keeffe D, Frazer K, Kemple M, ... O'Callaghan E (2015). Improving social functioning and reducing social isolation and loneliness among people with enduring mental illness: Report of a randomised controlled trial of supported socialisation. Int J Soc Psychiatry, 61(3), 241–250. doi: 10.1177/0020764014540150 [PubMed: 25001267]
- Sinokki M, Ahola K, Hinkka K, Sallinen M, Harma M, Puukka P, ... Virtanen M (2010). The association of social support at work and in private life with sleeping problems in the Finnish health 2000 study. J Occup Environ Med, 52(1), 54–61. doi: 10.1097/JOM.0b013e3181c5c373 [PubMed: 20042884]
- Soares A, Biasoli I, Scheliga A, Baptista RL, Brabo EP, Morais JC, ... Spector N (2013). Association of social network and social support with health-related quality of life and fatigue in long-term

survivors of Hodgkin lymphoma. Support Care Cancer, 21(8), 2153–2159. doi: 10.1007/s00520-013-1775-x [PubMed: 23475196]

- Steptoe A, Shankar A, Demakakos P, & Wardle J (2013). Social isolation, loneliness, and all-cause mortality in older men and women. Proc Natl Acad Sci U S A, 110(15), 5797–5801. doi: 10.1073/ pnas.1219686110 [PubMed: 23530191]
- Sun GW, Shook TL, & Kay GL (1996). Inappropriate use of bivariable analysis to screen risk factors for use in multivariable analysis. J Clin Epidemiol, 49(8), 907–916 [PubMed: 8699212]
- Tomaka J, Thompson S, & Palacios R (2006). The Relation of Social Isolation, Loneliness, and Social Support to Disease Outcomes Among the Elderly. Journal of Aging and Health, 18(3), 359–384. doi: 10.1177/0898264305280993 [PubMed: 16648391]

Victor CR, & Yang K (2012). The Prevalence of Loneliness Among Adults: A Case Study of the United Kingdom. The Journal of Psychology, 146(1–2), 85–104. doi: 10.1080/00223980.2011.613875 [PubMed: 22303614]

- Walton GM, & Cohen GL (2011). A brief social-belonging intervention improves academic and health outcomes of minority students. Science, 331(6023), 1447–1451. doi: 10.1126/science.1198364 [PubMed: 21415354]
- Winkleby MA, Jatulis DE, Frank E, & Fortmann SP (1992). Socioeconomic status and health: how education, income, and occupation contribute to risk factors for cardiovascular disease. American Journal of Public Health, 82(6), 816–820. doi: 10.2105/ajph.82.6.816 [PubMed: 1585961]
- Yu B, Steptoe A, Niu K, Ku PW, & Chen LJ (2018). Prospective associations of social isolation and loneliness with poor sleep quality in older adults. Qual Life Res, 27(3), 683–691. doi: 10.1007/ s11136-017-1752-9 [PubMed: 29188485]

#### Table 1a:

#### Characteristics of 2541 participants according to subjective social isolation

Variable	Low subjective social isolation (N=1365)	High subjective social isolation (N=1176)	Р*
Age (60–103 years), mean ± SD	$73.3\pm8.3$	$71.7\pm8.4$	< 0.001
Sex (female), %	44.5	49.1	0.02
Ethnicity (non-Euro-American), %	23.1	20.6	0.13
Education (12–17 years), mean ± SD	$15.5 \pm 1.7$	15.6 ± 1.7	0.58
Marital status (non-partnered), %	47.5	60.5	< 0.001
Employment status (retired), %	66.6	61.1	0.002
Body-mass index (10.8–94.6), mean $\pm$ SD	$26.2\pm4.8$	$26.6\pm5.2$	0.08
Charlson Comorbidity Index (2–21), mean $\pm$ SD	$5.4 \pm 2.9$	$5.2 \pm 2.9$	0.19
Number of alcoholic drinks per week (0–35), mean $\pm$ SD	$3.1\pm4.8$	$2.7 \pm 4.4$	0.03
Smoking (current smoker), %	4.5	6.5	0.03
Physical activity (less active than peers), %	11.7	20.0	< 0.001
Sleep quality (PSQI: 0–20), mean ± SD	$4.8 \pm 3.3$	$6.2 \pm 3.6$	< 0.001
Depression (CES-D: 0–10), mean ± SD	$1.0 \pm 1.4$	$2.3 \pm 2.2$	< 0.001
Fatigue (CFQ: Likert score $0-33$ ), mean $\pm$ SD	$12.0 \pm 3.2$	$13.0 \pm 3.6$	< 0.001
Sleep disturbance case (PSQI>5), %	34.1	50.0	< 0.001
Depression case (CES-D 4), %	6.4	25.3	< 0.001
Fatigue case (CFQ bimodal score 4), %	16.4	29.5	< 0.001

SD = standard deviation; PSQI = Pittsburgh Sleep Quality Index; CESD-D = 10-item Center for Epidemiological Studies Depression Scale; CFQ = Chalder Fatigue Questionnaire

Subjective social isolation represents loneliness and was dichotomized using the median split (loneliness score <4 vs. 4).

\* P-value from chi-square tests (for categorical variables) or t-tests (for continuous variables)

#### Table 1b:

#### Characteristics of 2541 participants according to objective social isolation

Variable	Low objective social isolation (N=1169)	High objective social isolation (N=1372)	Р*
Age (60–103 years), mean ± SD	$73.1\pm8.5$	$72.2\pm8.3$	0.006
Sex (female), %	46.7	46.5	0.92
Ethnicity (non-Euro-American), %	22.1	21.8	0.87
Education (12-17 years), mean (SD)	$15.6\pm1.6$	15.5 ± 1.7	0.03
Marital status (non-partnered), %	50.3	56.3	0.003
Employment status (retired), %	63.8	64.2	0.07
Body-mass index (10.8–94.6), mean $\pm$ SD	$26.3\pm5.0$	$26.4\pm5.0$	0.65
Charlson Comorbidity Index (2–21), mean ± SD	$5.3 \pm 2.8$	5.3 ± 2.9	0.98
Number of alcoholic drinks per week (0–35), mean $\pm$ SD	$3.2\pm4.8$	2.7 ± 4.5	0.02
Smoking (current smoker), %	4.8	5.9	0.22
Physical activity (less active than peers), %	12.5	18.1	< 0.001
Sleep quality (PSQI: 0–20), mean ± SD	$5.0 \pm 3.4$	5.7 ± 3.6	< 0.001
Depression (CES-D: 0–10), mean ± SD	$1.4 \pm 1.7$	$1.8 \pm 2.1$	< 0.001
Fatigue (CFQ: Likert score 0–33), mean $\pm$ SD	$12.3 \pm 3.4$	12.6 ± 3.5	0.04
Sleep disturbance case (PSQI>5), %	37.3	45.0	< 0.001
Depression case (CES-D 4), %	11.5	18.2	< 0.001
Fatigue case (CFQ bimodal score 4), %	20.2	24.4	0.01

SD = standard deviation; PSQI = Pittsburgh Sleep Quality Index; CESD-D = 10-item Center for Epidemiological Studies Depression Scale; CFQ = Chalder Fatigue Questionnaire

Objective social isolation was assessed using social network size and dichotomized using the median split (social network size 12 vs <12).

\* P-value from chi-square tests (for categorical variables) or t-tests (for continuous variables)

#### Table 2:

Associations of objective and subjective social isolation with behavioral symptoms before and after adjusting for each other (N=2541)

Dependent variable	Standardized beta <sup>*</sup> in separate models		Standardized beta <sup>**</sup> in the same models adjusting for each other		
Dependent variable	Social network size	Loneliness	Social network size	Loneliness	
Sleep disturbance	-0.10 (P<0.001)	0.25 (P<0.001)	-0.04 (P=0.03)	0.24 (P<0.001)	
Depressive symptoms	-0.11 (P<0.001)	0.44 (P<0.001)	-0.01 (P=0.48)	0.44 (P<0.001)	
Fatigue	-0.04 (P=0.04)	0.17 (P<0.001)	-0.003 (P=0.89)	0.17 (P<0.001)	

Objective social isolation was assessed using social network size and subjective social isolation represents loneliness.

\* Adjusted for age, sex, ethnicity, education, marital status, employment status, body-mass index, medical comorbidity, smoking, alcohol consumption, and physical activity

\*\* Adjusted for loneliness and social network size in addition to age, sex, ethnicity, education, marital status, employment status, body-mass index, medical comorbidity, smoking, alcohol consumption, and physical activity

#### Table 3:

Associations of the composite variable of objective and subjective social isolation with behavioral symptoms (N=2506)

	Standardized beta*			
Dependent variable	Low objective & low subjective isolation (n=639)	High objective & low subjective isolation (n=575)	Low objective & high subjective isolation (n=512)	High objective & high subjective isolation (n=780)
Sleep disturbance	Reference	0.07 (P=0.002)	0.17 (P<0.001)	0.22 (P<0.001)
Depressive symptoms	Reference	0.02 (P=0.42)	0.20 (P<0.001)	0.29 (P<0.001)
Fatigue	Reference	0.01 (P=0.60)	0.10 (P<0.001)	0.13 (P<0.001)

Objective social isolation was assessed using social network size and subjective social isolation represents loneliness. Categories were defined using median splits.

\* Adjusted for age, sex, ethnicity, education, marital status, employment status, body-mass index, medical comorbidity, smoking, alcohol consumption, and physical activity