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Loneliness, depression and cognitive function in older U.S. adults

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Abstract

Objective—To examine reciprocal relations of loneliness and cognitive function in older adults.

Methods—Data were analyzed from 8382 men and women, age 65 and older, participating in the US Health and Retirement Study from 1998 to 2010. Participants underwent biennial assessments of loneliness and depression (classified as no, low or high depression) determined by the Center for Epidemiologic Studies Depression scale (8-item version), cognition (a derived memory score based on a word list memory task and proxy-rated memory and global cognitive function), health status and social and demographic characteristics from 1998 to 2010. We used repeated measures analysis to examine the reciprocal relations of loneliness and cognitive function in separate models controlling sequentially and cumulatively for socio-demographic factors, social network, health conditions and depression.

Results—Loneliness at baseline predicted accelerated cognitive decline over 12 years independent of baseline socio-demographic factors, social network, health conditions and depression ($\beta = -0.2$, $p = 0.002$). After adjustment for depression interacting with time, both low and high depression categories were related to faster cognitive decline and the estimated effect of

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Previous presentation

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Conflicts of interest

The authors have no disclosures to report.

loneliness became marginally significant. Reciprocally, poorer cognition at baseline was associated with greater odds of loneliness over time in adjusted analyses (OR 1.3, 95% CI (1.1–1.5) $p = 0.005$), but not when controlling for baseline depression. Furthermore, cognition did not predict change in loneliness over time.

Conclusion—Examining longitudinal data across a broad range of cognitive abilities, loneliness and depressive symptoms appear to be related risk factors for worsening cognition but low cognitive function does not lead to worsening loneliness over time.

Keywords

loneliness; depression; memory; cognitive function; aging; longitudinal

Introduction

Loneliness is the perceived experience of social deprivation, distinct from objective social isolation, that has been associated with accelerated functional decline and increased mortality in older adults (Perissinotto *et al.*, 2012). Loneliness has also been found to predict greater cognitive decline over 4–10 years (Shankar *et al.*, 2013; Tilvis *et al.*, 2004) and a doubling of the risk of Alzheimer's disease (AD) dementia (Wilson *et al.*, 2007). These associations suggest that loneliness may be a behavioral response or prodromal symptom resulting from neurobiological changes because of cognitive disorders such as AD or loneliness may be a disease-modifying factor accelerating progression along causal pathways to cognitive impairment.

A number of instruments assessing loneliness have been developed, validated and implemented in studies of the elderly, such as the 20-item and 3-item versions of the UCLA Loneliness Scale and the De Jong-Gierveld Loneliness Scale (De Jong and Van Tilburg, 2006; Hughes *et al.*, 2004; Russell, 1996). Loneliness has also been measured using a single question from the Center for Epidemiologic Studies Depression Scale (CES-D) scale that asks study participants if they have felt lonely much of the time during the past week (Turvey *et al.*, 1999). The prevalence of loneliness experienced "often" or "much of the time" has ranged from 13 to 19% in samples of US adults, age 60 and older (Perissinotto *et al.*, 2012; Theeke, 2009). In comparable international cohorts, rates of loneliness ranging from 14 to 22% have been reported (Victor and Yang, 2012). Thus, understanding the role of loneliness and related neuropsychiatric factors in cognitive impairment and AD has the potential to significantly impact the cognitive health, quality of life and longevity of aging populations worldwide.

Currently, the relation of loneliness to depression, and their impact on cognition in late life, are only partially understood. Although loneliness is highly correlated with depression scores (Cacioppo *et al.*, 2010) and unmarried status (Theeke, 2009) most lonely older individuals are married, live with others and are not clinically depressed (Perissinotto *et al.*, 2012). In cross-sectional studies of community-dwelling elderly, evidence for a significant relationship of loneliness and cognitive function, independent of depression, has been mixed (Boss *et al.*, 2015). In analyses from the Dublin Healthy Ageing study, loneliness was associated with poorer performance on tests of processing speed, category fluency, visual

memory and short delay verbal memory, independent of case-level depression defined by a structured clinical interview (O'Luanaigh *et al.*, 2012). In contrast, in the Lothian Birth Cohort study, investigators found that loneliness was not associated with general cognitive ability, processing speed or memory performance controlling for depression as a continuous measure (Gow *et al.*, 2013).

Longitudinal trajectories of loneliness, depression and cognition are also not well defined. While it appears that loneliness may be an independent risk factor for cognitive decline (Shankar *et al.*, 2013), prior studies have not clearly established if this association persists when rigorously controlling for high levels of depression, an established risk factor for mild cognitive impairment (MCI) (Barnes *et al.*, 2006; Geda *et al.*, 2006; Palmer *et al.*, 2007; Steenland *et al.*, 2012) and dementia (Rosenberg *et al.*, 2013), or even low levels of depression which may also carry increased risk of progression to MCI (Barnes *et al.*, 2006). Findings from the Rush Memory and Aging project indicated that repeated measures of loneliness defined as an "enduring loneliness" variable predicted global cognitive decline, controlling for baseline depression, but analyses did not examine loneliness over time and depression over time as equivalent predictors of longitudinal cognition (Wilson *et al.*, 2007). Close examination of the effects of loneliness and depression, together over time, may be informative, as loneliness could be a risk factor or clinical marker, upstream of depression, leading to cognitive decline via common disease mechanisms.

Causal associations of loneliness and low cognitive function are also uncertain. Loneliness has rarely been examined as a manifestation or consequence of cognitive impairment, rather than an antecedent risk factor, in epidemiological studies (Wilson *et al.*, 2007).

The objective of this study was to examine the reciprocal relations of loneliness and cognitive function in older adults, adjusting for social network, depression and other demographic and health-related factors. We hypothesized that the relation of loneliness and poor cognition would be bi-directional and that loneliness would be significantly associated with poor cognition as both a risk factor and an outcome over 12 years, independent of demographic factors, social network, health conditions and depression.

Methods

Participants

Data were derived from the Health and Retirement Study (HRS), a nationally representative cohort collecting information on the health, social, work and economic characteristics of older adults in the United States that has been conducted biennially since 1992 (Herringa and Connor, 1995; Juster and Suzman, 1995). The target population for the HRS national area probability sample includes all adults, over age 50, living in households in the contiguous United States. HRS is funded through the National Institute of Aging (U01AG009740) and is administered by the University of Michigan Institute for Social Research. Data are publically available through the HRS website (http://hrsonline.isr.umich.edu/).

For these analyses, we examined longitudinal data from 1998 to 2010. Our analyses were restricted to non-Hispanic white and black participants, age 65 and older in 2000 (i.e. the first year of outcome), who completed cognitive and clinical assessments in 1998 and at one or more follow up surveys. From 10,817 age-eligible participants in the 1998 HRS sample, we excluded 954 (8.8%) missing baseline exposure in 1998, 1198 (11.1%) missing a memory outcome in 2000, 283 (2.6%) missing a key baseline covariate, yielding a final analytic sample of 8382 respondents (Sample 1). Compared with the final analytical sample, the excluded sample were older (mean = 75.9 years), had more males (52.0%), black participants (12.8%), lower income and fewer years of education (mean = 11.0 years). At subsequent waves, those who were older, male, white and had more years of education were more likely to drop out either because of mortality or non-participation. We adjusted for such attrition in subsequent waves using inverse probability weighting (see the statistical analyses section).

For the analysis of the effect of cognition on loneliness as the outcome, the final analytical sample contained 8030 respondents after excluding those missing baseline exposure, baseline covariates or loneliness outcome in 2000.

Assessments of loneliness and depression

Loneliness and depression were evaluated using the CES-D, 8-item version (Turvey *et al.*, 1999) that asks participants to indicate whether each of eight symptoms was present or absent “much of the time during the past week” (each item rated 0 if not present or 1 if present). Specifically, questions probed whether respondents “felt depressed”, “felt that everything was an effort”, had “restless sleep”, “were happy”, “felt lonely”, “enjoyed life”, “felt sad” or “could not get going.” Loneliness was rated as present if participants responded affirmatively to the loneliness question. Modified CES-D scoring was used to exclude the loneliness question in order to derive a separate depression score that was calculated as the sum of the remaining seven questions (possible range 0–7). Depression was modeled as a categorical variable that included “no depression” (score=0) as the reference term, “low depression” (score=1–2) or “high depression” category (score=3–7) corresponding to 42%, 38% and 20% of the sample respectively at baseline in 1998. The “high depression” cutoff was defined *a priori* by inspection of the score distribution within the sample and was informed by the threshold for clinically significant depression used in prior research (Moon *et al.*, 2014). “Low depression” was conceptualized as a subclinical or subthreshold depression group.

Cognitive assessments

Baseline cognitive function was heterogeneous in this population-based cohort. Memory/cognitive performance was directly assessed using a 10-word list test of immediate and delayed memory from the Telephone Interview for Cognitive Status (Brandt and Folstein, 1988). For participants who were too impaired to undergo direct testing, proxy respondents rated the participant’s memory using a 5-point Likert scale and completed the 16-item version of the Informant Questionnaire for Cognitive Decline (IQCODE) that assesses global cognitive function including memory and new learning, orientation, attention, comprehension, mathematical and reasoning abilities (Jorm, 1994; Jorm *et al.*, 2000;

Ofstedal *et al.*, 2005). Use of proxy respondents was determined by either the participant, a gatekeeper (usually a spouse or family member) or, sometimes, by the interviewer if performance on cognitive tests was extremely poor. We previously developed a continuous, derived memory score that combines direct and proxy data, allowing for longitudinal analyses across a broad range of cognitive abilities (Wu *et al.*, 2013). This method provides coefficient estimates for direct and proxy measures and other predictors on a linear scale in which positive coefficients are associated with better memory/cognitive performance. Using these coefficient estimates, a derived memory score can then be calculated for all HRS participants based on direct or proxy scores and other demographic information. This approach provides a continuous assessment of memory/cognition that includes individuals with low cognitive function who are unable to perform direct assessments and, thus, reduces attrition bias.

Assessments of socio-demographic variables, social network and health conditions

Baseline socio-demographic information included age, sex, race (white, black, Hispanic or other), education (years of completed schooling, 0–17), household wealth and household income. A social network score was calculated as the sum of 4 dichotomous domain scores, based on whether the participant (i) was married or living with a partner; (ii) had at least weekly contact with friends or neighbors; (iii) had at least weekly contact with a child and (iv) participated in a volunteer activity in the past year. An index of medical illness was calculated as the number of conditions (hypertension, diabetes, cancer, pulmonary disease, heart disease and stroke) that were queried by self-report (each scored 0 or 1, total range 0–6, greater number indicates more morbidity).

Statistical analyses

Two series of analyses were performed to examine the reciprocal relations of loneliness and cognitive function. In a series of models examining loneliness as a predictor of cognition over 12 years (Series A), we controlled sequentially and cumulatively for (i) socio-demographic factors (age, sex, race, years of education, wealth, income); (ii) social network; (iii) health conditions and (iv) depression. An analogous set of models analyzed cognition as a predictor of loneliness over time (Series B). For loneliness predicting cognition (Series A) a final model added depression interacting with time as a covariate.

We estimated generalized linear models with robust variance to account for repeated measures on the same individual. All longitudinal analyses were adjusted for potential bias because of selective loss to follow-up and mortality using inverse probability weights (IPW) (Hernan *et al.*, 2004). For each wave, we estimated the probabilities that a respondent who was alive at the prior wave survived to the current wave, and also participated in the current wave, as a function of the respondent's characteristics at the prior wave. The product of probabilities at each wave was used to compute the cumulative probability of surviving to a given wave and participating in the study in that wave. The inverse of such probability was the IPW, and can be incorporated in the regression model to adjust for selective attrition because of survival and other forms of loss-to-follow-up (Weuve *et al.*, 2012). SAS Version 9.2 (Cary, NC) was employed for all analyses.

Results

Baseline characteristics of the sample (n = 8382) are shown in Table 1. Overall, 17.6% of the total sample endorsed feeling "lonely much of the time during the last week." Compared to the non-lonely, those endorsing loneliness at baseline were significantly older, were more likely to be female, unmarried and black. On average, the lonely group also had lower educational attainment, household income and wealth and had a lower baseline cognitive score (see Table 1). Depressive symptoms were common, with 38% reporting low (1–2) symptoms and 20% reporting high (3–7) depressive symptom levels compared to 42% with no depressive symptoms. Among the lonely, mean CES-D (minus loneliness) score at baseline was significantly higher than among the non-lonely (means: 2.80 vs. 0.95, $p<$ 0.001).

Trajectory of change in cognition associated with loneliness

Controlling cumulatively for socio-demographic variables, social network, health conditions and baseline depression in models 1–4, greater baseline loneliness interacting with time was a significant predictor of worsening cognition (for loneliness interacting with time in models 1–4, β =−0.2, 95% CI (−0. 3, −0.1), p=0.002). Therefore, the estimated rate of cognitive decline was 20% higher over 10 years in the lonely compared to the non-lonely individuals. Both low and high baseline categorical depression (compared to no depression) were also significantly associated with worsening cognition (see Table 2, Models 1–4). In the final model that included baseline depression interacting with time among the predictor terms, the interaction of loneliness and time became marginally significant as a predictor of worsening cognition (β =−0.1, 95% CI (−0.2, 0.01) p = 0.08). Compared to no depression, both low and high categorical depression variables interacting with time were found to be significant predictors of worsening cognition (for low depression interacting with time, β =−0.08, 95% CI (0.14, −0.02), p = 0.01; for high depression interacting with time β =−0.2, 95% CI (−0.28, −.06), p = 0.003) (see Table 2, Model 5).

Trajectory of change in loneliness associated with cognition

In serial models controlling sequentially for socio-demographic variables, social network and health conditions, poorer baseline cognition was significantly associated with greater odds of loneliness across time (OR =1.35, p = 0.005; see Table 3, Models 1–3). The association of poorer cognition and greater loneliness was not significant, however, adjusting for baseline depression (see Table 3, Model 4). Similarly, poorer health was associated with greater odds of loneliness in Model 3, but this association was not statistically significant in the subsequent model controlling for baseline depression. In the final model, greater age, female sex, lower education, less wealth, low social network and depression were all significantly associated with greater odds of loneliness across time (see Table 3, Model 4). This pattern of findings contrasts with the prior reciprocal model: the relation of low cognition and subsequent loneliness appears to be stable across time rather than a pattern in which low cognition leads to increasing loneliness. Furthermore, low cognition does not appear to independently predict loneliness over time when accounting for baseline depression.

Discussion

Examining the reciprocal relations of loneliness and cognition in a large cohort of older US adults, we found that greater loneliness at baseline was associated with accelerated cognitive decline over 12years independent of established socio-demographic risk factors (greater age, female sex, low education, low socioeconomic status) and other significant factors such as low social network, poor health and greater baseline depression. In adjusted analyses, the estimated rate of cognitive decline was approximately 20% faster in the lonely compared to the non-lonely group. Roughly half of the lonely group endorsed no depression or only subthreshold depressive symptoms at baseline while the remaining half scored above the predetermined cutoff for significant depression. Thus loneliness was not uniformly associated with clinical depression and had significant effects on long-term cognition independent of baseline depression burden. Therefore, as a predictive, clinically measurable variable, loneliness has utility in identifying older individuals at elevated risk of cognitive decline. Both low and high depression categories were significantly associated with faster cognitive decline (as indicated by the interaction of depression score with time) and the estimated effect of loneliness on the rate of cognitive decline was marginally significant in models adjusted for the impact of depressive symptoms on cognitive decline. This suggests that the causal effects of loneliness and depression on cognitive decline are not distinct. Thus, the loneliness symptom as measured by the CES-D, low depression (defined as the endorsement of one or two depressive symptoms), and high depression (defined as three to seven symptoms) appeared to be related predictors of cognitive decline. Reciprocally, when examining cognition as a predictor of loneliness and controlling for baseline depression, lower baseline cognitive score was not associated with greater odds of loneliness and did not predict changes in loneliness over time. Collectively, these findings suggest that loneliness and other depressive symptoms hasten cognitive decline over time but low cognitive function does not lead to worsening loneliness.

Our findings add to a small number of studies addressing loneliness and depression together and their differential impact on cognition in late life. A prior clinical-pathologic study of non-demented elderly found that loneliness was not only associated with more rapid decline in global cognition but also increased incident AD dementia, diagnosed clinically, over 4 years (Wilson *et al.*, 2007). Using a modified version of the de Jong-Gierveld loneliness scale to define loneliness, and controlling for CES-D depression score on a continuous scale, there was a 40% increased risk of AD dementia diagnosis in lonely compared to non-lonely individuals. Repeated measures of loneliness, modeled as an enduring loneliness variable, were longitudinally related to more rapid declines in global cognition, controlling for numerous socio-demographic variables, social network and engagement, physical and activity levels and baseline depressive symptoms. Models were not adjusted for an equivalent enduring depression variable or for an interaction term for depression and time, which may explain more independent effects for loneliness compared to depression in their work when compared to our own. As in our study, they found that global cognition did not predict change in loneliness over time.

Analyses from the English Longitudinal Study of Ageing provide other evidence for loneliness as an independent risk factor for cognitive decline. Using the 3-item version of the

UCLA Loneliness Scale, greater baseline loneliness, adjusted for continuous CES-D depression scores, predicted declines in delayed recall and immediate recall but not verbal fluency over 4 years (Shankar *et al.*, 2013). The effect of loneliness on delayed recall was modified by low education and by social isolation indicating that loneliness may be particularly useful as a predictor in high-risk older adults with low social and cognitive reserves. By comparison, depression as a continuous measure was significantly associated with lower immediate and delayed recall and verbal fluency controlling for loneliness and other relevant covariates. Three-item UCLA scores were moderately correlated with CES-D depression scores at baseline (r =0.4, $p < 0.001$) demonstrating construct overlap but not identity. As in our own work, social isolation and low wealth were high risk factors in all models underscoring the importance of these exogenous factors to cognitive health.

While the specific impact of loneliness on cognitive function is an emerging area of research, in comparison, there is now strong evidence relating greater depressive symptoms to increased progression from normal cognition to MCI and from MCI to dementia (Donovan *et al.*, 2014; Geda *et al.*, 2014; Rosenberg *et al.*, 2013). In line with these studies, we found that high depression, defined as a categorical variable, was strongly associated with cognitive decline, consistent with prior work demonstrating a doubling of the risk of progression from normal cognition to MCI in those scoring at or above cutoffs for clinically significant depression on depression rating instruments (Geda *et al.*, 2006; Steenland *et al.*, 2012).

Notably, we add to prior work by demonstrating that even low depression (endorsement of only one or two depressive symptoms) at baseline was associated with accelerated cognitive decline, suggesting that depression-related pathophysiological effects appear to be continuous and present at the lowest levels detectable with standard depression rating scales. This finding adds to emerging evidence that very low depressive symptoms are significant predictors of transition to MCI (Barnes *et al.*, 2006) and potential markers of neurodegenerative brain changes (Donovan *et al.*, 2015) in older adults with normal cognition. An outstanding question is whether clinicians' attention should be focused on loneliness or particular depressive symptoms that may have special utility in predicting adverse outcomes such as cognitive and functional impairment.

Our work supports an understanding of loneliness as an easily measured marker of emotional and social distress, closely aligned with, and possibly prodromal to depression. Interpersonal loss, particularly when paired with social rejection, is a long-recognized and potent risk factor for the development of major depression (Kendler *et al.*, 2003). Extending this association more specifically to loneliness, a recently published network model of CES-D depressive symptoms suggested that loneliness may critically activate other depressive symptoms in the setting of late-life bereavement (Fried *et al.*, 2015). Similarly, in a 5-year observational study of older adults, greater loneliness, using the 20-item UCLA scale, was found to significantly predict greater CES-D depression scores, but not the converse (Cacioppo *et al.*, 2010). Collectively, these findings and other biological studies point to loneliness as a proxy marker of psychosocial stress and prodromal symptom of depression, mediated by pro-inflammatory alterations in central nervous system activity and possibly, direct neural effects on motivational systems and dopaminergic pathways (Pizzagalli, 2014).

Thus loneliness may be a modifiable risk factor, along with subclinical depressive symptoms and major depression, with downstream effects on cognitive health via shared pathophysiological mechanisms.

A potential limitation of this study was the use of a simple, binary measure of loneliness that may be a less sensitive measure of loneliness compared to the 3-item UCLA instrument. This may have biased our results toward the null in detecting associations with cognition in both reciprocal models. Compared with other loneliness metrics, the CES-D loneliness measure may also less effectively disambiguate loneliness and depression constructs thereby underestimating a possible independent effect of loneliness on cognition and the converse. Our approach to using CES-D depression as a categorical variable with “high depression” and “low depression” groups is not typical as a continuous depression score or a dichotomous “case-level” depression variable are more commonly used. However, this categorical variable allowed us to analyze non-zero values of depressive symptoms at levels below cutoff for clinical depression thereby revealing significant effects of subthreshold symptoms on longitudinal cognition. Our study did not account for acute versus chronic loneliness that may involve different physiological, neurobiological and clinical correlates and outcomes. In addition, data was not available to classify participants by baseline cognitive status (normal cognition, MCI, dementia) and it is possible that loneliness may manifest differently and have different relevance as a risk factor or a symptom across progressive stages of cognitive impairment. Thus, while our methods reduced attrition bias and allowed for the examination of loneliness and cognition across a broad range of cognitive function, proxy or behavioral rather than verbal self-report measures may more accurately detect psychosocial distress akin to loneliness in later stages of dementia progression.

Conclusion

We examined loneliness and cognition over 12 years in a large population-based cohort of older adults and found that loneliness significantly predicted worsening cognitive function independent of socio-demographic factors, social network, poor health and baseline depression but not when controlling for the effect of depression over time. Reciprocally, lower baseline cognitive function predicted greater loneliness but not when adjusting for baseline depression. These results highlight loneliness as a clinical marker of social and emotional distress that appears to be etiologically linked to depression and cognitive decline in older adults. Further longitudinal analyses utilizing more refined loneliness measures and biological markers are necessary to define temporal and causal relations of loneliness, depression, and dementia in late life. Understanding pathogenic mechanisms and disease pathways associated with acute and chronic loneliness may reveal novel psychotherapeutic and biological therapies to enhance global health, longevity and quality of life for older adults.

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Key points

- One out of six older US adults reported feeling lonely much of the time during the past week.
- Being lonely was associated with a 20% faster rate of cognitive decline over 12 years, controlling for baseline depression and other important confounders, whereas, in reciprocal models, low cognitive function did not independently predict future loneliness.
- High and even subclinical depressive symptoms were also related to accelerated cognitive decline, effects that diminished the independent effect of loneliness.
- Loneliness may be a modifiable risk factor, along with subclinical depressive symptoms and major depression, with downstream effects on cognitive health.

Table 1

Baseline demographic and clinical data

	Total sample	Lonely	Non-lonely	*p* Value[a]
Number of subjects	8382	1483	6899	
Age in years, mean	73.20 (6.47)	74.96 (7.02)	72.82 (6.28)	<0.001
Male sex (%)	40	30	42	<0.001
Years of education, mean	12.21 (2.82)	11.33 (3.02)	12.40	<0.001
Black race (%)	8	11	7	<0.001
Married or living with a partner (%)	58	26	65	<0.001
Wealth quintile (%)				<0.001
1st (lowest)	14	24	11	
2nd	17	21	17	
3rd	21	21	21	
4th	23	19	24	
5th (highest)	25	15	27	
Income quintile (%)				<0.001
1st (lowest)	21	31	19	
2nd	10	10	10	
3rd	24	24	23	
4th	24	21	25	
5th (highest)	21	14	23	
CES-D minus loneliness				
Categories (%)				
0	43	13	49	
1–2	38	34	39	
3–7	19	53	12	
Social network	1.7 (0.92)	1.26 (0.85)	1.79 (0.91)	<0.001
Health conditions index	1.16 (1.00)	1.37 (1.08)	1.11 (0.98)	<0.001
Cognition/derived memory score	0.78 (0.57)	0.62 (0.65)	0.82 (0.55)	<0.001

All estimates were weighted by baseline sampling weight.

CES-D Center for Epidemiologic Studies Depression Scale, 8-item version: total depression score was derived from 7 items, excluding the loneliness item. Social network score was derived as the sum of 4 domains based on marriage, contacts with friends and neighbors, contacts with children and participation in volunteer activities. Health conditions index was calculated as the number of self-reported medical conditions (hypertension, diabetes, cancer, pulmonary disease, heart disease and stroke).

[a] Comparison was based on two-sample *t*-test or chi square test.

Table 2

SERIES A: Serial longitudinal models of baseline loneliness and select covariates (1998) predicting global cognitive score over time (2000–2010)

Predictor	Model 1 Demographics	Model 2 (+Social network)	Model 3 (+ Health conditions)	Model 4 (+ Depression)	Model 5 (+Depression interacting with time)
Loneliness interacting with time	β =−0.2 (−0.3, −0.1) p = 0.002	β =−0.2 (−0.3, −0.1) p = 0.002	β =−0.2 (−0.3, −0.1) p = 0.002	β =−0.2 (−0.3, −0.1) p = 0.002	β =−0.1 (−0.2, 0.01) p = 0.08
Social network		β =−0.3 p < 0.0001	β =−0.3 p < 0.0001	β =−0.3 p < 0.0001	β =−0.2 p < 0.0001
Health conditions			β =−0.3 p = 0.0005	β =−0.3 p = 0.003	β =−0.2 p = 0.003
Low Categorical depression (1–2)				β =−0.26 p = 0.048	β =0.08 p = 0.6
High Categorical depression (3–7)				β =−1.0 p < 0.0001	β =−0.3 p = 0.13
Low Depression interacting with time					β =−0.08 p = 0.01
High Depression interacting with time					β =−0.2 p = 0.003
Loneliness	β = 0.03 p = 0.9	β = 0.02 p = 0.3	β = 0.02 p = 0.3	β = 0.05 p = 0.01	β = 0.03 p = 0.2
Time	β =−0.7 p < 0.0001	β =−0.7 p < 0.0001	β =−0.7 p < 0.0001	β =−0.7 p < 0.0001	β =−0.6 p < 0.0001
Age	β = −0.7 p < 0.0001	β = −0.7 p < 0.0001	β = −0.7 p < 0.0001	β = −0.7 p < 0.0001	β = −0.7 p = 0.01
Sex (male)	β = −2.0 p < 0.0001	β = −0.2 p < 0.0001	β = −0.2 p < 0.0001	β = −0.2 p < 0.0001	β = −0.2 p < 0.0001
Race (African American)	β = −4.8 p < 0.0001	β = −4.8 p < 0.0001	β = −4.8 p < 0.0001	β = −4.8 p < 0.0001	β = −4.8 p < 0.0001
Years of education	β = 0.3 p < 0.0001	β = 0.3 p < 0.0001	β = 0.3 p < 0.0001	β = 0.3 p < 0.0001	β = 0.3 p < 0.0001
Wealth Quintile 4 (highest)	Reference				
Quintile 3	β = 0.09 p = 0.6	β = 0.1 p = 0.5	β = 0.1 p = 0.5	β = 0.1 p = 0.4	β = 0.1 p = 0.4
Quintile 2	β = −0.4 p = 0.08	β = −0.3 p = 0.2	β = −0.3 p = 0.2	β = −0.3 p = 0.2	β = −0.3 p = 0.2
Quintile 1	β = −0.6 p = 0.02	β = −0.5 p = 0.06	β = −0.4 p = 0.1	β = −0.4 p = 0.1	β = −0.4 p = 0.1
Quintile 0 (lowest)	β = −1.0 p = 0.002	β = −1.0 p = 0.002	β = −1.0 p = 0.003	β = −1.0 p = 0.003	β = −1.0 p = 0.003

Predictor	Model 1 Demographics	Model 2 (+Social network)	Model 3 (+ Health conditions)	Model 4 (+ Depression)	Model 5 (+Depression interacting with time)
Income Quintile 4 (highest)	Reference				
Quintile 3	$\beta = -0.4$ $p = 0.01$	$\beta = -0.4$ $p = 0.02$	$\beta = -0.4$ $p = 0.02$	$\beta = -0.4$ $p = 0.02$	$\beta = -0.4$ $p = 0.02$
Quintile 2	$\beta = -0.2$ $p = 0.4$	$\beta = -0.2$ $p = 0.4$	$\beta = -0.2$ $p = 0.4$	$\beta = -0.1$ $p = 0.4$	$\beta = -0.1$ $p = 0.4$
Quintile 1	$\beta = -0.5$ $p = 0.08$	$\beta = -0.5$ $p = 0.08$	$\beta = -0.5$ $p = 0.1$	$\beta = -0.4$ $p = 0.1$	$\beta = -0.4$ $p = 0.1$
Quintile 0 (lowest)	$\beta = -1.0$ $p = 0.0003$	$\beta = -0.9$ $p = 0.0003$	$\beta = -0.9$ $p = 0.0007$	$\beta = -0.8$ $p = 0.001$	$\beta = -0.8$ $p = 0.001$

Depression was defined as the sum of 7 items derived from the Center for Epidemiologic Studies Depression (CES-D) Scale, 8-item version, excluding the loneliness item. Low Depression (1–2) and High Depression (3–7) were categorical variables, classified in relation to No Depression (0). Loneliness was defined by the corresponding binary item on the CES-D Scale. Social network score was derived as the sum of 4 domains based on marriage, contacts with friends and neighbors, contacts with children and participation in volunteer activities. Health conditions index was calculated as the number of self-reported medical conditions (hypertension, diabetes, cancer, pulmonary disease, heart disease and stroke). The unit of time is 10 years.

Table 3

SERIES B: Serial longitudinal models of baseline global cognition and select covariates (1998) predicting loneliness over time (2000–2010)

Predictor	Model 1 Demographics	Model 2 (+Social network)	Model 3 (+ Health conditions)	Model 4 (+ Depression)
Low baseline cognition	OR = 1.3 (1.1, 1.6) $p = 0.004$	OR = 1.3 (1.1, 1.5) $p = 0.007$	OR = 1.3 (1.1,1.5) $p = 0.005$	OR = 1.1 (0.9,1.3) $p = 0.3$
Low cognition interacting with time	OR = 1.02 (0.98, 1.05) $p = 0.23$	OR = 1.02 (0.98, 1.05) $p = 0.26$	OR = 1.02 (0.98, 1.05) $p = 0.37$	OR = 1.02 (0.98, 1.05) $p = 0.37$
Social network		OR = 0.9 $p < 0.0001$	OR = 0.8 $p < 0.0001$	OR = 0.8 $p < 0.0001$
Health conditions			OR = 1.1 $p = 0.001$	OR = 1.0 $p = 0.2$
Low categorical depression (1–2)				OR = 1.8 $p < 0.0001$
High categorical depression (3–7)				OR = 4.2 $p < 0.0001$
Time (year)	OR = 1.05 $p = 0.02$	OR = 1.04 $p = 0.04$	OR = 1.04 $p = 0.07$	OR = 1.04 $p = 0.05$
Age	OR = 1.02 $p = 0.0002$	OR = 1.01 $p = 0.007$	OR = 1.01 $p = 0.02$	OR = 1.02 $p < 0.0001$
Sex (male)	OR = 0.64 $p < 0.0001$	OR = 0.67 $p < 0.0001$	OR = 0.66 $p < 0.0001$	OR = 0.77 $p < 0.0001$
Race (African American)	OR = 0.76 $p = 0.008$	OR = 0.79 $p = 0.02$	OR = 0.80 $p = 0.03$	OR = 0.84 $p = 0.09$
Years of education	OR = 0.93 $p < 0.0001$	OR = 0.93 $p < 0.0001$	OR = 0.93 $p < 0.0001$	OR = 0.95 $p < 0.0001$
Wealth Quintile 4 (highest)	Reference			
Quintile 3	OR = 1.2 $p = 0.01$	OR = 1.2 $p = 0.02$	OR = 1.2 $p = 0.03$	OR = 1.1 $p = 0.3$
Quintile 2	OR = 1.5 $p < 0.0001$	OR = 1.4 $p = 0.0001$	OR = 1.4 $p = 0.0003$	OR = 1.4 $p = 0.0004$
Quintile 1	OR = 1.4 $p = 0.0002$	OR = 1.4 $p = 0.003$	OR = 1.3 $p = 0.007$	OR = 1.3 $p = 0.03$
Quintile 0 (lowest)	OR = 2.1 $p < 0.0001$	OR = 1.9 $p < 0.0001$	OR = 1.9 $p < 0.0001$	OR = 1.7 $p < 0.0001$
Income Quintile 4 (highest)	Reference			
Quintile 3	OR = 1.1 $p = 0.2$	OR = 1.1 $p = 0.2$	OR = 1.1 $p = 0.2$	OR = 1.2 $p = 0.05$
Quintile 2	OR = 1.1 $p = 0.3$	OR = 1.1 $p = 0.2$	OR = 1.1 $p = 0.2$	OR = 1.1 $p = 0.2$
Quintile 1	OR = 1.1 $p = 0.5$	OR = 1.1 $p = 0.5$	OR = 1.1 $p = 0.6$	OR = 1.1 $p = 0.6$
Quintile 0 (lowest)	OR = 1.4 $p = 0.002$	OR = 1.3 $p = 0.006$	OR = 1.3 $p = 0.01$	OR = 1.2 $p = 0.06$

Depression was defined as the sum of 7 items derived from the Center for Epidemiologic Studies Depression (CES-D) Scale, 8-item version, excluding the loneliness item. Low Depression (1–2) and High Depression (3–7) were categorical variables, classified in relation to No Depression (0). Loneliness was defined by the corresponding binary item on the CES-D Scale. Social network score was derived as the sum of 4 domains based on marriage, contacts with friends and neighbors, contacts with children and participation in volunteer activities. Health conditions index was calculated as the number of self-reported medical conditions (hypertension, diabetes, cancer, pulmonary disease, heart disease and stroke).