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Loneliness is associated with risk of cognitive impairment in the Survey of Health, Ageing and Retirement in Europe

Running Head: LONELINESS AND COGNITIVE IMPAIRMENT

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Abstract

Objectives: To test whether loneliness is associated with risk of cognitive impairment up to 11 years later in a European sample of middle-aged and older adults. The study examines whether this association is independent of measures of social isolation, depression and other risk factors for cognitive impairment and dementia.

Methods: Participants (N = 14,114) from the Survey of Health, Ageing and Retirement in Europe (SHARE) answered a single item on loneliness at baseline and were assessed for cognitive impairment every two-to-three years for 11 years. Participants who scored at least 1.5 standard deviations below the age-graded mean on both a memory recall task and verbal fluency task were classified as impaired. A 3-item measure of loneliness was available for a sample of respondents followed up to 4 years.

Results: Feeling lonely was associated with increased risk of incident cognitive impairment (HR = 1.31, 95%CI = 1.19-1.44), after accounting for age, sex, education, and SHARE country strata. The association was robust but reduced in magnitude when controlling for clinical and behavioral risk factors, health-related activity limitations, social isolation, social disengagement and depressive symptoms. The association was not moderated by socio-demographic factors and was also apparent when using the 3-item loneliness scale instead of the single-item measure.

Conclusions: These findings expand the extant literature on loneliness and risk of cognitive impairment in older adulthood. Loneliness is one modifiable factor that can be intervened on prior to the development of severe impairment or dementia.

Keywords: loneliness, incident cognitive impairment, psycho-social risk factors, social isolation.

Key points:

- This study tests the association between loneliness and cognitive impairment over time.
- Feeling lonely increased the risk of developing cognitive impairment up to 11 years later.
- The association remained significant accounting for clinical and behavioral risk factors, health-related activity limitations, social isolation and depressive symptoms.
- Higher risk of cognitive impairment was still apparent after excluding participants with five years or less of follow-up.

Introduction

Loneliness is a significant public health concern in our aging society.[1] Feelings of loneliness are associated with worse health in general and with poor cognitive function and risk of developing Alzheimer's disease and dementia in particular.[2–4] Loneliness is not the mere absence of social contacts but rather the negative feeling that arises when there is a discrepancy between one's desired and perceived quality of social relationships.[5,6] In a recent study of American adults (N = 12,030, age ≥ 50), we found a robust association between loneliness and incident dementia: For each 1-point increase in loneliness, participants had a 40% increased risk of developing dementia over the 10-year follow-up.[7] More importantly, the association held when controlling for measures of social isolation, depression, and other clinical (e.g., diabetes) and behavioral (e.g., physical activity) factors associated with late-life cognition.[8,9] Lara and colleagues [10] recently conducted a meta-analysis of 8 studies (including ours) that evaluated the association between loneliness and dementia risk. The results of this meta-analysis supported the primary studies that found that feeling lonely increased dementia risk (RR = 1.26; 95% CI = 1.14, 1.40) and also pointed to the heterogeneity of effect sizes across studies (I^2 = 23; 95% CI = 0, 63). Three out of eight studies in the meta-analysis found no association between loneliness and incident dementia.[11–13] Interestingly, some studies found loneliness to increase risk of cognitive impairment preceding dementia [13,14] and the transition from mild to more severe impairment.[7] Because cognitive impairment might be an early marker of dementia and other neurodegenerative conditions, these results underscore the importance to examine cognitive impairment (not exclusively dementia) in relation to loneliness. There are, however, inconsistent results for those few studies that examined cognitive impairment and/or cognitive decline as the outcome.[3,14–17] Wilson and colleagues,[3] for example, found a more rapid decline in cognitive performance over four years for participants who felt lonely, even after accounting for measures of social network and depression. Wang and colleagues, in contrast, found no evidence of an association between loneliness and changes in cognitive status or transition from normal to mild or severe cognitive impairment in their 20-year cohort study.[16]

Despite increased interest in the topic, the relation between loneliness and late-life cognition is not as well understood as those of other risk factors for cognitive impairment (such as diabetes or education).[10] There are many factors that are hypothesized to underlie and modulate the association.[7,10] For example, individuals who feel lonely might engage in fewer health-promoting behaviors, such as social[18] or physical activities,[19,20] and be more likely to experience depressed affect,[21,22] which are all factors that are may contribute to changes in cognitive function in old age.[9,22] Loneliness and its associated risks might also be prevalent for specific groups of individuals, such as women or un-married adults.[23] However, results are inconsistent for interactions with these socio-demographic factors.[7,15] The purpose of this work is to add to the literature by examining the relation between loneliness and cognitive impairment in one of the largest longitudinal cohort studies in Europe: the Survey of Health, Ageing and Retirement in Europe (SHARE).[24] Consistent with studies on dementia, we hypothesize that loneliness will be associated with risk of incident cognitive impairment among adults over the age of 50. We examine this association over a relatively long follow-up (up to 11 years) and control for potential mediators or confounding factors: social isolation/disengagement, health-related activity limitations, depressive symptoms, and other behavioral and clinical risk factors for cognitive impairment and dementia. Lastly, we test whether the association varies by age, sex, education level, and marital status.

Method

Participants and Procedure

The current study makes use of the SHARE, a cross-national multi-disciplinary study of individuals aged 50 and older and their spouses across Europe.[24] We used data from Wave 1 (fieldwork completed between 2004-06; DOI: 10.6103/SHARE.w1.700) as our baseline assessment because this wave was the first to include a question on loneliness as part of the drop-off questionnaire. Cognitive function was assessed as part of the in-person interview at baseline and at the following waves: Wave 2 (2006-10), Wave 4 (2011-12), Wave 5 (2013) and Wave 6 (2015) (DOIs: 10.6103/SHARE.w2.700, 10.6103/SHARE.w4.700, 10.6103/SHARE.w5.700, 10.6103/SHARE.w6.700; see Footnote 1). Participants were selected into the analytic sample if they had loneliness measured in 2004-06 (baseline), did not have cognitive impairment at that time (see below), and had at least one follow-up cognitive assessment through the 2015 assessment. A total of 18,272 had complete data at baseline (including data on age, sex, and education level). Of these participants, 3,861 did not have follow-up data (1,128 died before a follow-up assessment). There were no differences in loneliness between those with and without follow-up, though those who did not have a follow-up scored lower on cognition at baseline. The main analyses are based on 14,114 respondents across 12 countries: Austria, Belgium, Denmark, France, Germany, Greece, Italy, Spain, Sweden, Switzerland, the Netherlands and Israel. A 3-item measure of loneliness was subsequently included in SHARE as part of the 2011-12 (Wave 4) drop-off questionnaire (see Footnote 1 for details on study design). We used this measure to conduct a secondary analysis on SHARE participants who had data on loneliness at the 2011-12 wave, no cognitive impairment at that time and had cognition re-assessed in at least one of the two following waves (either 2013 or 2015). The analysis was restricted to participants from the same countries assessed at Wave 1, except for Israel and Greece, which did not participate in Wave 4.

SHARE is reviewed and approved by the Ethics Committee of the University of Mannheim and the Ethics Council of the Max Planck Society. More information on the assessment, sampling, and how to obtain the data can be found at: http://www.share-project.org.

Measures

Loneliness

At the 2004-06 baseline, participants completed a single-item measure of loneliness as part of the abbreviated version of the Center for Epidemiological Studies Depression scale. They were asked: "How often have you experienced the following feelings over the last week: I felt lonely?" (see Footnote 2). Response options were: 1 = Almost all of the time; 2 = Most of the time; 3 = Some of the time; 4 = Almost none of the time. This item was reverse scored in the direction of greater loneliness. This measure was used for our primary analysis of cognitive impairment to ensure a relatively long follow-up. In 2011-12, SHARE included a 3-item version of the UCLA loneliness scale.[25,26] Participants reported how much of the time they felt a lack of companionship, felt left out, and felt isolated from others, on a 3-point scale: 1 = often, 2 = some of the time, 3 = hardly ever or never. Responses were reverse-scored and the mean taken across the items (alpha reliability = .78). This measure was used for a secondary follow-up analysis to allow comparison of results when using single vs. multi-item measures of loneliness.

Cognitive Impairment

To classify cognitive impairment, we used a standard approach used in prior studies with SHARE.[27,28] At each wave, participants were asked to complete a memory recall task (immediate and delayed recall of 10 common words) and an animal fluency task (naming as much animals as

possible in 60 seconds).[25] Participants who performed 1.5 standard deviations (SD) below the age-graded mean of either immediate or delayed recall (or both) were coded as 1 and compared to other participants, coded 0. Similarly, those who performed 1.5 SD below the age-graded mean of verbal fluency were coded as 1 and compared to others, coded 0. Those who reported "don't know" for any task were coded 1 as well. Cognitive impairment was defined as scoring 1 on both the memory and verbal fluency tasks.

Social Isolation

In line with prior studies,[29,30] we computed indicators of social isolation: being single, separated from spouse, divorced, or widowed (yes/no), having rare contact with children or no children (yes/no), and household size (3+ members, 2 members, or only 1 member). SHARE also asked whether respondents, in the last month, had participated in voluntary or charity work, attended an educational or training course, gone to a sport, social or other kind of club, or taken part in a political or community-related organization.[25,29,30] A sum score of these activities was computed and then reversed in the direction of social disengagement (from 0 = Engaged in all five activities to 5 = Engaged in none of the activities).

Covariates

Age (years), sex (0 = male, 1 = female), and educational level (from 0 = Pre-primary education to 6 = Second stage of tertiary education) were used as basic covariates. SHARE used the 1997 International Standard Classification of Education to categorize and harmonize education statistics across European countries. Information on participants' country was available, but not information on race/ethnicity. Additional risk factors and covariates included clinical and behavioral covariates, health-related activity limitations, and depression symptoms. Clinical covariates were body mass index (kg/m^2) and reported diagnosis of hypertension (yes/no) and diabetes (yes/no). Behavioral covariates were frequency of moderate physical activity (reverse scored, with responses ranging from 1 = hardly ever or never to 4 = more than once a week) and smoking status (yes/no). Health-related limitations were assessed with the Global Activity Limitations Index (i.e., "For the past 6 months at least, to what extent have you been limited because of a health problem in activities people usually do?"; the item was reverse scored, with responses ranging from 1 = not limited to 3 = severely limited).[31] Depressive symptoms were assessed by the EURO-D scale,[32] which measured 12 symptoms (yes/no): depressed mood, pessimism, suicidality, guilt, troubles with sleep, loss of interest, irritability, change in appetite, fatigue, concentration, enjoyment, and tearfulness (sum of 12 items ranged from 0-12). All covariates were from the baseline assessment. We further computed two dummy-coded variables to detect transition into widowhood (yes/no) and increases in health-related limitations (yes/no) over the follow-up. These variables were included as covariates in supplemental analyses, as these factors potentially increase risk for cognitive impairment.[33]

Statistical Approach

Cox regression hazard models were used to test whether loneliness at baseline was associated with incident cognitive impairment over up to 11 years of follow-up. This approach was used because it evaluates time-to-event from baseline predictors. That is, it evaluates the occurrence of an event (cognitive impairment) considering the time from the predictor of interest (loneliness) to the first instance of the event. Time was coded in years from the baseline assessment as years-to-incidence. For participants who did not score impaired, cases were censored at the last available cognitive assessment. The strata function was used to account for the nested nature of the data (i.e., participants within countries). The Kaplan-Meier plot indicated no violation of the proportionality assumption. We first tested loneliness as a predictor of

incident cognitive impairment, controlling for age, sex and education (Model 1). To test whether the association was independent of other common risk factors, we repeated the analyses controlling for behavioral and clinical risk factors (Model 2), health-related activity limitations (Model 3), indicators of social isolation and social disengagement (Model 4), and depressive symptoms (Model 5). Finally, we tested interaction terms to examine whether the association varied by participant age, sex, education level, or marital status. In supplemental analyses, we also tested whether the association between loneliness and impairment persisted after controlling for widowhood across the follow-up period and changes in health limitations.

To test the robustness of the association, we performed four sensitivity analyses: (1) we repeated the analyses restricting the sample to participants aged 65 and older to ensure the association was not solely due to the lower prevalence of impairment below age 65; (2) we excluded participants with 5 or fewer years of follow-up to account for possible reverse causality (that is, loneliness as a consequence of cognitive impairment); (3) we limited the analyses to countries that participated in all waves of SHARE (9 countries participated in all waves); and (4) we selected participants who were socially engaged (i.e., those who engaged in at least one of the five social activities) and tested whether loneliness was still associated with cognitive impairment in this group.

Lastly, a follow-up analysis was conducted with participants who completed the 3-item UCLA scale in 2011-12. This analysis was performed to test whether the association between loneliness and cognitive impairment was dependent on the scale used to assess loneliness. It included participants who had loneliness and cognition assessed in 2011-12 and at least one follow-up assessment of cognition in 2013 or 2015 (n = 23,339; M age = 65.32, SD = 9.57; 55.6% females). We ran a cox regression model with the UCLA scale predicting risk of cognitive impairment, controlling for the basic covariates. The follow-up period for this analysis was 4 years (see Footnote 3 for further details).

Results

Descriptive statistics for the main longitudinal sample are shown in Table 1. Over the up to 11-year follow-up period (116,120 person years), 525 participants (3.6%) developed cognitive impairment. Results of the Cox regression models are reported in Table 2. For every 1-point increase in loneliness, there was a 31% increased risk of cognitive impairment over the follow-up, after controlling for age, sex, and education. Comparing the top and bottom of the loneliness item, participants who reported feeling lonely almost all the time had the double of the risk of impairment compared to participants who reported never feeling lonely (HR = 2.07, 95% CI = 1.46-2.95; n = 9,697). The association was independent of clinical and behavioral risk factors (Model 2), health-related activity limitations (Model 3), social isolation and social disengagement (Model 4), and depressive symptoms (Model 5). The association remained significant but was reduced by about 50% in the fully-adjusted model. There was no moderation by age, sex, education, or marital status (ps >.05). The association was still significant when further controlling for widowhood (HR = 1.35, 95% CI = 1.22-1.49) or increases in health-related limitations across the follow-up (HR = 1.23, 95% CI = 1.11-1.35).

Sensitivity analyses indicated that the association was robust: It remained significant when the sample was restricted to participants 65 years and older (HR = 1.24, 95% CI = 1.08–1.43), when participants with 5 or fewer years of follow-up were excluded (HR = 1.30, 95% CI = 1.17–1.46), and when the sample was limited to participation in all SHARE waves (HR = 1.35, 95% CI = 1.14–1.60). In the last sensitivity analysis, we focused on participants who were

socially engaged (i.e., those engaged in at least one of the specified social activities). Among this group (n = 6,179), loneliness was still associated with increased risk of cognitive impairment (HR = 1.32, 95% CI = 1.07–1.63), after accounting for age, sex and education.

Finally, the association was also apparent with the 3-item loneliness scale. In the follow-up analysis, 2.5% of participants (560/23,339) scored in the cognitive impairment range over the 4-year follow-up (80,838 person years). With the 3-item scale, loneliness was associated with an over 50% increased risk of cognitive impairment (HR=1.56, 95% CI = 1.32-1.84). Further details for this analysis are reported in Footnote 3.

Discussion

The present research provides evidence that feeling lonely is a risk factor for cognitive impairment in middle-age and older adulthood. Loneliness was associated with higher risk of cognitive impairment up to 11 years later. The association was robust and remained significant (though reduced) when accounting for indicators of social isolation/disengagement, health-related limitations, and depressive symptoms. It was also significant after accounting for widowhood and changes in health status over the follow-up. Moreover, the association did not vary by age, sex, education, nor marital status.

These findings are consistent with prior studies.[13–15] Wilson and colleagues,[3,14] for example, found loneliness and negative social interactions to be associated with cognitive impairment and steeper decline in multiple cognitive domains (semantic memory, perceptual speed, and visuospatial ability). As noted above, however, some studies reported non-significant associations between loneliness and cognitive outcomes.[16, 17] It is of note that these latter studies examined specific age groups (oldest-old)[16] and used different definitions of cognitive status and/or cognitive tasks.[17]

Loneliness may increase risk of cognitive impairment in several ways. Lonely individuals tend to suffer from hypertension[34] and other health problems[35] that can harm cognitive health. Individuals higher in loneliness also tend to engage in health-risk behaviors, including physical inactivity[19,20] and smoking[36] that are also risk factors for cognitive impairment.[9] In addition, loneliness is related to heightened psycho-physiological reactivity to stress and depression,[21,37] which are factors related to dementia.[38,39] McHugh Power and colleagues,[22] for example, found depressive symptoms to be one mediator of the relation between loneliness and cognitive function. Other mediators, however, need to be identified and tested in future work. In our sample, the association between loneliness and cognitive impairment was reduced in size when accounting for risk factors such as depressive symptoms. Nonetheless, the association was still apparent, which suggests that the factors considered here are not the sole pathways through which loneliness increases risk for cognitive impairment.

Loneliness may also derive from social isolation and health-related activity limitations. Yet, feelings of loneliness are not unique to persons who live alone or have few social contacts. A person may feel lonely even if not alone and this feeling may have long-term detrimental effects on cognition. In contrast, engagement in social and simulating activities, such as participation in games, sports or community-related activities, may help to maintain cognitive function and reduce loneliness feelings over time.[40]

Loneliness may also be a manifestation of progressive cognitive impairment rather than a risk factor. In the current study, however, the association persisted when excluding participants who became impaired within the first five years of follow-up, whose loneliness may have been a consequence of severe cognitive impairment. Nonetheless, there still may be possible reciprocal

relations between loneliness and cognition.[41] Further, changes in both loneliness and cognition may be reactive to changes in health status[42] and loss of partners.[43] Supplemental analysis in the current study, however, suggests that the association between loneliness and cognitive impairment is apparent even after controlling for widowhood and declines in health status.

The present research has several strengths, including the large sample size, the relatively long follow-up (up to 11 years), and the testing of multiple nested models. The study also supports the utility of using single-item screening questions to detect risk factors such as loneliness in community populations. Such an assessment is valid [44,45] and has predictive power for risk of dementia up to several years later.[4] Yet, there are limitations and possibilities for future research. First, research would benefit from measures that capture different dimensions of loneliness, such as emotional loneliness (i.e., felt absence of an intimate partner) and social loneliness (i.e., felt absence of social networks).[5] In fact, emotional loneliness may be the component that is more relevant for individuals' health rather than social loneliness.[46] It would be interesting to examine both loneliness dimensions in association with cognitive outcomes. Second, the current study did not have information on a clinical diagnosis of dementia or differential diagnosis for mild versus severe cognitive impairment. Future studies should combine multiple measures to ascertain cognitive status, as well as brain-related biomarkers. Two studies, for example, showed that cognitively intact individuals who felt lonely had higher levels of amyloid and tau, two proteins that accumulate in the brain of Alzheimer's patients.[47,48] Third, although we examined the association between loneliness and cognitive impairment in a different cultural context than what has been studied previously (Europe compared to the US[3,14] and Asia[15]), there might be variability in levels of loneliness that might depend on cultural differences between European regions and countries.[49] Lastly, even though the study covered a 11-year period, longer follow-ups with multiple assessments of loneliness are needed to better rule out reverse causality, to determine whether there are critical periods for loneliness (e.g., middle adulthood versus early old age), and whether there are changes in loneliness leading to dementia.

Despite these limitations, this research indicates a robust association between loneliness and risk of cognitive impairment in middle age and older adulthood. The results underscore the importance of paying attention to loneliness and to identifying interventions that may reduce feelings of loneliness prior to the development of severe impairment and dementia.

Footnotes

Footnote 1: SHARE is an ongoing study. At each wave, new participants are recruited from the original 12 European countries that participated in Wave 1 and from new countries that joined the survey later on (nine new countries joined the study across Wave 2 to Wave 6). In the current study, the sample included participants from those countries for which we had data on loneliness at baseline. Wave 3 and Wave 7 applied a life story interview and were not considered for the current analyses.

Footnote 2: At the 2004-06 baseline, the loneliness item was translated consistently across countries. The only exception was for the Netherlands. In this country, the translation of the item was 'I felt alone'. When excluding Dutch participants, the association between loneliness and cognitive impairment remained significant in all statistical models, except Model 5 (that accounted for depression).

Footnote 3: Because of the inclusion of re-fresh samples, a higher number of participants had data on the 3-item loneliness scale in 2011-12. Of those with data on the 3-item loneliness scale, about 25% (n = 5,679) were part of the longitudinal sample tested at the 2004-06 baseline. When restricting the analysis to this sub-sample, loneliness was still significantly associated with risk of cognitive impairment over the 4-year follow-up (HR = 1.65, 95% CI = 1.14-2.39). The 2011-12 wave also included a single-item question of loneliness: How much of time do you feel lonely? (3-point response). This measure was highly correlated with the 3-item UCLA scale (r = .73). When using the single-item instead of the 3-item scale, the hazard ratio was 1.28 (95% CI = 1.12-1.46) across the 4 years.

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Table 1

Descriptive Statistics for the Full Sample and by Cognitive Status at Follow-up

	Total Sample	*No Cognitive Impairment*	*Cognitive Impairment*	*Chi-square or t-test*
N	14,411	13,886	525	--
Age in years	63.61 (9.33)	63.61 (9.33)	63.60 (9.31)	ns
Age≥65	6,128 (42.5%)	5,895 (42.5%)	233 (44.4%)	ns
Sex				
Females	54.7%	54.7%	56.2%	ns
Males	45.3%	45.3%	43.8%	
Marital Status				
Married	74.1%	74.0%	77.0%	ns
Non-married	25.9%	26.0%	23.0%	
Education Level				
Pre-primary education	4.2%	4.0%	11.6%	***
Primary education	27.3%	26.6%	43.6%	
Lower secondary education	17.8%	17.9%	15.4%	
Upper secondary education	27.8%	28.2%	18.5%	
Post-secondary education	2.8%	2.9%	1.3%	
First stage tertiary education	19.8%	20.2%	9.3%	
Second stage tertiary education	0.3%	0.3%	0.2%	
Loneliness at baseline	1.48 (0.75)	1.47 (0.74)	1.73 (0.91)	***
1 - Almost none of the time	64.3%	64.8%	51.2%	
2 - Some of the time	26.9%	26.7%	31.4%	
3 - Most of the time	5.5%	5.3%	10.1%	
4 - Almost all the time	3.4%	3.2%	7.2%	
Cognitive Scores at Baseline				
Immediate Word Recall (0-10)	5.04 (1.69)	5.08 (1.68)	3.95 (1.70)	***
Delayed Word Recall (0-10)	3.55 (1.91)	3.59 (1.90)	2.54 (1.84)	***
Verbal Fluency (0-90+)	19.46 (6.95)	19.66 (6.92)	14.40 (5.71)	***
Cognitive Scores at Follow-up				
Immediate Word Recall (0-10)	4.87 (1.87)	4.99 (1.76)	1.56 (1.54)	***
Delayed Word Recall (0-10)	3.51 (2.17)	3.63 (2.12)	0.57 (0.97)	***
Verbal Fluency (0-90+)	18.20 (7.87)	18.71 (7.52)	4.64 (3.31)	***

Note. Unadjusted means (standard deviations) or cases (percentages) are reported. Higher scores on loneliness indicated higher feelings of loneliness. Standardized mean differences (*d*s) in cognitive performance between baseline and follow-up were calculated for each group. For participants without cognitive impairment, d = -.05 for immediate recall, d = .02 for delayed recall and d = -.13 for verbal fluency; for participants with an impairment, d = -1.48 for immediate recall, d = -1.41 for delayed recall and d = -2.16 for verbal fluency. Austria N = 1,047 (3.3% with cognitive impairment [35 cases]); Belgium N = 2,010 (1.8% with impairment [37 cases]); Denmark N = 932 (1.5% with impairment [14 cases]); France N = 847 (3.5% with impairment [30 cases]), Germany N = 1,108 (2.1% with impairment [23 cases]); Greece N = 1,592 (6.1% with impairment [97 cases]); Italy N = 1,084 (7.5% with impairment [81 cases]);

Spain N = 1,113 (10.8% with impairment [120 cases]); Sweden N = 1,623 (1.2% with impairment [20 cases]); Switzerland N = 525 (0.6% with impairment [3 cases]); the Netherlands = 1,351 (1.2% with impairment [16 cases]); Israel N = 1,179 (4.2% with impairment [49 cases]). * p <.05, ** p ≤.01, *** p ≤.001, ns = non-significant difference.

Table 2

Loneliness and Cognitive Impairment over 11-year follow-up

Variable	Model 1	Model 2	Model 3	Model 4	Model 5
Age	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (0.98-1.01)	1.01 (0.99-1.02)	1.00 (0.99-1.02)
Female	0.87 (0.73-1.04)	0.85 (0.71-1.02)	0.84 (0.70-1.01)	0.93 (0.75-1.17)	0.86 (0.68-1.08)
Education level	0.79 (0.73-0.84)***	0.81 (0.75-0.87)***	0.82 (0.76-0.88)***	0.84 (0.76-0.91)***	0.83 (0.76-0.91)***
Body mass index	--	1.00 (0.98-1.02)	1.00 (0.97-1.02)	1.01 (0.98-1.03)	1.01 (0.98-1.03)
Hypertension	--	0.99 (0.82-1.20)	0.97 (0.80-1.18)	0.89 (0.71-1.12)	0.90 (0.71-1.14)
Diabetes	--	1.47 (1.15-1.90)**	1.41 (1.10-1.82)**	1.38 (1.02-1.87)*	1.36 (1.00-1.85)*
Physical activity	--	0.78 (0.72-0.85)***	0.80 (0.74-0.87)***	0.84 (0.76-0.92)***	0.85 (0.77-0.94)***
Smoking	--	1.00 (0.79-1.26)	1.00 (0.79-1.26)	0.99 (0.75-1.31)	0.97 (0.73-1.28)
Health-related activity limitations	--	--	1.25 (1.09-1.43)***	1.22 (1.04-1.43)*	1.16 (0.98-1.37)
Single, separated or widowed	--	--	--	0.84 (0.60-1.18)	0.86 (0.61-1.21)
Rare contact or no children	--	--	--	1.12 (0.80-1.56)	1.11 (0.79-1.55)
Small household size	--	--	--	0.96 (0.83-1.11)	0.96 (0.83-1.12)
Social disengagement	--	--	--	1.43 (1.19-1.71)***	1.41 (1.17-1.69)***
Depressive symptoms	--	--	--	--	1.07 (1.02-1.13)**
Loneliness	1.31 (1.19-1.44)***	1.24 (1.12-1.38)***	1.23 (1.11-1.36)***	1.24 (1.09-1.41)***	1.15 (1.01-1.32)*
N	14,337	14,086	14,085	10,022	9,961

Note. Hazard ratios and 95% confidence intervals are reported. N varies across models due to missing values on covariates; cases censored before the earliest event in a stratum were automatically dropped from the analyses.
* $p < .05$, ** $p \leq .01$, *** $p \leq .001$.