Psychological Medicine

cambridge.org/psm

Social relationship factors, depressive symptoms, and incident dementia: a prospective cohort study into their interrelatedness

Lukas A. Duffner[1], Kay Deckers[1], Dorina Cadar[2,3], Marjolein E. de Vugt[1] and Sebastian Köhler[1]

[1]Alzheimer Centrum Limburg, Mental Health and Neuroscience Research Institute (MHeNS), Department of Psychiatry and Neuropsychology, Faculty of Health, Medicine and Life Sciences, Maastricht University, The Netherlands; [2]Department of Behavioural Science and Health, Institute of Epidemiology and Health, University College London, UK and [3]Department of Neuroscience, Centre for Dementia Studies, Brighton and Sussex Medical School, Brighton, UK

Original Article

Cite this article: Duffner LA, Deckers K, Cadar D, de Vugt ME, Köhler S (2024). Social relationship factors, depressive symptoms, and incident dementia: a prospective cohort study into their interrelatedness. *Psychological Medicine* **54**, 3115–3125. https://doi.org/10.1017/S0033291724001272

Received: 11 October 2023
Revised: 21 February 2024
Accepted: 9 May 2024
First published online: 4 September 2024

Keywords:
cohort study; dementia; depressive symptoms; factor analysis; prevention; public health; risk reduction; social relationships; structural equation modeling

Corresponding author:
Sebastian Köhler;
Email: s.koehler@maastrichtuniversity.nl

Abstract

Background. Different aspects of social relationships (e.g., social network size or loneliness) have been associated with dementia risk, while their overlap and potentially underlying pathways remain largely unexplored. This study therefore aimed to (1) discriminate between different facets of social relationships by means of factor analysis, (2) examine their associations with dementia risk, and (3) assess mediation by depressive symptoms.

Methods. Thirty-six items from questionnaires on social relationships administered in Wave 2 (2004/2005) of the English Longitudinal Study of Ageing ($n = 7536$) were used for exploratory and confirmatory factor analysis. Factors were then used as predictors in Cox proportional hazard models with dementia until Wave 9 as outcome, adjusted for demographics and cardiovascular risk factors. Structural equation modeling tested mediation by depressive symptoms through effect decomposition.

Results. Factor analyses identified six social factors. Across a median follow-up time of 11.8 years (IQR = 5.9–13.9 years), 501 people developed dementia. Higher factor scores for frequency and quality of contact with children (HR = 0.88; $p = 0.021$) and more frequent social activity engagement (HR = 0.84; $p < 0.001$) were associated with lower dementia risk. Likewise, higher factor scores for loneliness (HR = 1.13; $p = 0.011$) and negative experiences of social support (HR = 1.10; $p = 0.047$) were associated with higher dementia risk. Mediation analyses showed a significant partial effect mediation by depressive symptoms for all four factors. Additional analyses provided little evidence for reverse causation.

Conclusions. Frequency and quality of social contacts, social activity engagement, and feelings of loneliness are associated with dementia risk and might be suitable targets for dementia prevention programs, partly by lowering depressive symptoms.

Introduction

Dementia is an ongoing public health concern that will affect 153 million people worldwide by 2050 (Nichols et al., 2022). Global efforts to lower the number of future cases are twofold and consist of developing curative treatments as well as identifying behavioral targets for primary prevention and risk reduction. In this regard, research into modifiable risk factors has gained momentum, and it is suggested that a substantial proportion of future dementia cases could theoretically be delayed or prevented by addressing such factors (Livingston et al., 2020). Potential targets include the management of health conditions, such as hypertension, obesity, and hearing loss, but also lifestyle-related factors, including physical inactivity, unhealthy diet, or low social contact (Deckers et al., 2015; Livingston et al., 2020).

With regard to the latter, research suggests that different aspects of social relationships may be protective against cognitive decline and dementia. For example, studies have shown that people who frequently engage in social leisure activities or are members of clubs/organizations have a lower risk of developing dementia, independent of other dementia risk factors (Almeida-Meza, Steptoe, & Cadar, 2021; Duffner et al., 2022). Similarly, larger social networks, higher quality of social relationships, and lower levels of loneliness and social isolation have been associated with lower dementia risk (Amieva et al., 2010; Kuiper et al., 2015; Samtani et al., 2022). Some of those 'social relationship constructs' are ill-defined, based on face validity and highly overlapping, but so far, no studies have addressed this potential overlap psychometrically by studying the existence of overarching latent constructs.

Insight into possible pathways of the association between social relationship factors and dementia risk may help identify the most beneficial 'social targets' and is thus of major relevance for the design of future prevention programs and health initiatives. However, relatively few studies have addressed the putative causal structure between different social relationship factors and dementia risk. For instance, while socio-emotional factors, such as depressive symptoms, have been suggested as potential mediators of the association between social relationship factors and dementia risk, no study has formally tested these pathways (John, Patel, Rusted, Richards, & Gaysina, 2019; Qiao et al., 2022). This also includes the possibility of reverse causation, in that impending dementia is the cause rather than the result of changes in social relationships (Bielak & Gow, 2022; Floud et al., 2021).

There is thus a need to examine which and how social relationship factors might explain dementia risk. The current study, therefore, aims to identify meaningful constructs of social relationships using factor analysis (research question 1); to examine the association between identified constructs and incident dementia (research question 2), and to determine whether depressive symptoms mediate these associations (research question 3). It also aims to assess the possibility of reverse causation between identified factors and incident dementia (research question 4).

Methods

Study design and participants

Study participants were drawn from the English Longitudinal Study of Ageing (ELSA), a multi-center, observational cohort study launched in 2002 (Steptoe, Breeze, Banks, & Nazroo, 2013a). Data collection took place in bi-annual waves and included information about health status, socioeconomic position, social well-being, lifestyle, and cognition. Details about the sampling procedure and data collection have been published previously (Steptoe et al., 2013a). Participants have been initially selected to be representative of the general English population aged 50 years and older. The current study used data from Wave 2 (2004/2005) as baseline, as this is the first wave where an in-depth assessment of social relationship variables was conducted. Participants were followed up biannually until Wave 9 (2018/2019), resulting in a maximum observational period of 15 years. Of the initial 8780 participants, those with prevalent dementia at baseline (until Wave 2; $n = 45$) and without follow-up ($n = 1199$) were excluded. The analytical sample thus included 7536 participants. All participants provided their informed consent and the ELSA data collection protocol was approved by the National Research Ethics Service, in accordance with the Declaration of Helsinki.

Measures

Dementia ascertainment

Dementia was ascertained by a combination of either self-reported physician-diagnosed dementia (possible/probable Alzheimer's disease or an unspecified subtype) or a score of 3.38 or higher on the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE; Jorm, 1994). In the IQCODE, a close contact person of the participant rates changes (from 1-*much improved* to 5-*much worse*) in everyday cognitive functioning over a period of two years, based on 16 questions (e.g., 'Ability to remember what day/month it is compared to last interview'), responses to which are averaged to arrive at the final rating. The IQCODE has been well-validated across several populations and has shown good psychometric properties with regard to the chosen cutoff. More specifically, the IQCODE has been found to discriminate between people with a clinical diagnosis of dementia and those without with a sensitivity of 0.80 and a specificity of 0.84 (Quinn et al., 2021).

Social relationship items

A set of 36 items pertaining to various aspects of social relationships, including loneliness, was selected for factor analysis from questionnaires administered at Wave 2 based on their use in the operationalization of several social constructs in previous ELSA publications (Duffner et al., 2022; Fancourt, Steptoe, & Cadar, 2020; Khondoker, Rafnsson, Morris, Orrell, & Steptoe, 2017; Rafnsson, Orrell, D'Orsi, Hogervorst, & Steptoe, 2020). Table 1 contains an overview of all included items, along with the overarching constructs used in such previous studies. Items were phrased either in a dichotomous (yes/no) fashion or on a Likert scale with four to six response options.

Depressive symptoms

The eight-item version of the Center for Epidemiological Studies–Depression (CES-D) questionnaire was used to assess depressive symptoms. The CES-D assesses affective and somatic symptoms in the general population and has shown excellent psychometric properties (Radloff, 1977). Items are rated in a dichotomous manner and then added up, resulting in a theoretical range of 0–8, with higher scores indicating more symptoms related to depression. A detailed overview of the symptoms assessed by the CES-D is included in online Supplementary Table 1.

Demographics and health conditions

Baseline age and gender were used as covariates in all analyses. Furthermore, we incrementally controlled for the socioeconomic and cardiovascular risk factors outlined below. The selection of covariates was based on a pragmatic choice of factors having a known association with both social relationship factors and dementia.

Education. Self-reported levels of education (i.e., the highest educational level achieved) were clustered into high (college/university education), medium (ordinary level or secondary education), and low (no formal education).

Wealth. Household net-wealth was estimated by subtracting open payments and mortgages from all self-reported possessions, including the value of the participant's home, physical wealth, and other assets. Tertiles were subsequently created, representing high, medium, and low wealth.

Coronary heart disease. Self-reported, diagnosed angina pectoris, or myocardial infarction up to Wave 2 were used as measures of coronary heart disease. Both measures were collected retrospectively at the Wave 3 (2006/2007) assessment.

Hypertension. A combination of self-reported, diagnosed hypertension (assessed retrospectively at Wave 3), and mean systolic and diastolic blood pressure, measured at the Wave 2 nurse visit, were used. In line with guidelines of the World Health Organization and the International Society of Hypertension, a mean systolic blood pressure of $\geqslant$140 mm Hg or mean diastolic blood pressure of $\geqslant$90 mm Hg were regarded as indicative of hypertension (Unger et al., 2020; Whitworth, 2003).

Diabetes. Self-reported, diagnosed type-1 or type-2 diabetes or high blood glucose levels (assessed at Wave 3) or a blood glycated hemoglobin level of $\geqslant$6.5% (48 mmol/mol) at the Wave 2 nurse

https://doi.org/10.1017/S0033291724001272 Published online by Cambridge University Press

Table 1. Items assessing social relationship factors as presented in the ELSA Wave 2 dataset, along with their operationalization in previous ELSA publications

Construct	Item name	Description	Measurement scale
Having a partner (Fancourt et al., 2020)	SCPTR	*Whether has a husband, wife or partner with whom they live*	Dichotomous (yes/no)
Social isolation (Rafnsson et al., 2020; Steptoe et al., 2013b)	SCCHDG	*How often the respondent meets up with their children*	Seven-point Likert scale from 0 (never) to 6 (three or more times per week)
	SCCHDH	*How often the respondent speaks on the phone to their children*	
	SCCHDI	*How often the respondent writes to or emails their children*	
	SCFAMG	*How often the respondent meets up with other relatives*	
	SCFAMH	*How often the respondent speaks with other relatives on the phone*	
	SCFAMI	*How often the respondent writes to or emails other relatives*	
	SCFRDG	*How often the respondent meets up with their friends*	
	SCFRDH	*How often the respondent speaks with their friends on the phone*	
	SCFRDI	*How often the respondent writes to or emails their friends*	
	SCORG09	*Organizational membership: none*	Dichotomous (yes/no)
Social activities (Duffner et al., 2022)	SCACTA	*How often respondent goes to the cinema*	Six-point Likert scale from 1 (never) to 6 (twice per month or more)
	SCACTB	*How often respondent eats out of the house*	
	SCACTC	*How often respondent goes to an art gallery or museum*	
	SCACTD	*How often respondent goes to the theatre, a concert or the opera*	
	WPACTVW	*Whether volunteered last month*	Dichotomous (yes/no)
Social support by children (Khondoker et al., 2017)	SCCHDA	*How much the children understand the way the respondent feels about things*	Four-point Likert scale from 1 (not at all) to 4 (a lot)
	SCCHDB	*How much the respondent can rely on their children if they have a problem*	
	SCCHDC	*How much the respondent can open up to their children about their worries*	
	SCCHDD	*How much their children criticize the respondent*	
	SCCHDE	*How much their children let the respondent down when they are counting on them*	
Social support by other family (Khondoker et al., 2017)	SCFAMA	*How much do family members understand how respondent feels about things*	Four-point Likert scale from 1 (not at all) to 4 (a lot)
	SCFAMB	*How much respondent can rely on other relatives if they have a serious problem*	
	SCFAMC	*How much respondent can open up to these other relatives if they need to talk*	
	SCFAMD	*How much other relatives criticize the respondent*	
	SCFAME	*How much other relatives let the respondent down*	
Social support by friends (Fancourt et al., 2020; Khondoker et al., 2017)	SCFRDA	*How much these friends understand how respondent feels about things*	Four-point Likert scale from 1 (not at all) to 4 (a lot)
	SCFRDB	*How much respondent can rely on these friends if they have a serious problem*	
	SCFRDC	*How much respondent can open up to these friends if they need to talk*	
	SCFRDD	*How much these friends criticize the respondent*	
	SCFRDE	*How much these friends let the respondent down*	
Loneliness (Rafnsson et al., 2020; Steptoe et al., 2013b)	SCFEELA	*How often respondent feels they lack companionship*	Three-point Likert scale from 1 (hardly ever or never) to 3 (often)
	SCFEELB	*How often respondent feels left out*	
	SCFEELC	*How often respondent feels isolated from others*	
	SCFEELD	*How often respondent feels in tune with the people around them*	
	PSCEDE	*Whether respondent felt lonely much of the time during the past week*	Dichotomous (yes/no)

https://doi.org/10.1017/S0033291724001272 Published online by Cambridge University Press

visit were used in conjunction for inferring diabetes (World Health Organization, 2011).

Statistical analysis

Baseline differences in demographic characteristics between people with and without dementia were assessed using *t*-tests or χ^2-tests.

Factor analyses

To study the overlap between different social relationship measures and to identify meaningful latent constructs (i.e., data-reduction; research question 1), factor analyses were conducted in Mplus (Muthén & Muthén, 2017). For this, we first followed an unrestrained (exploratory factor analysis; EFA) approach, with the goal of identifying a maximum number of social constructs. Based on the results of this EFA, we then conducted a confirmatory factor analysis (CFA). Unlike EFA, where items are allowed to load across all factors, CFA imposes further restrictions. More specifically, items were initially restrained to load only the factors with the highest factor loadings in EFA. While in a traditional sense, a CFA may imply the replication of findings in a different sample, here we refer to a factor analysis with the imposition of further restrictions in the same sample.

In both EFA and CFA, model fit was assessed through χ^2 values, the root mean square error of approximation (RMSEA), the comparative fit index (CFI), and the non-normed fit index (i.e., Tucker–Lewis Index; TLI). A non-significant χ^2 value, RMSEA $\leqslant$0.07 and CFI and TLI $\geqslant$0.90 were used as indicative of acceptable model fit for both exploratory and confirmatory factor analyses (Hooper et al., 2008).

Exploratory factor analysis. After the examination of zero-order correlations, all social relationship items were imported into Mplus (Muthén & Muthén, 2017). Given the expected non-orthogonal (i.e., interrelated) factor structure, an OBLIMIN rotation was chosen. The minimally significant factor loading for an item to be retained was set to |0.4|, reflecting a rather liberal approach in conformity with previous studies (Peterson, 2000). Items below this threshold were dropped iteratively, starting with the lowest-loading item, and loadings were re-examined after removal. Eigenvalues were then examined, and factor solutions with a value of $\geqslant$1.0 were retained for individual inspection. Following a parsimonious approach, the solution with the lowest number of factors that was theoretically sound and had an acceptable model fit was subsequently used for confirmatory factor analysis.

Confirmatory factor analysis. The EFA factor solution was then tested in a CFA. In this CFA, depression was included as a latent factor, comprised of the eight items of the CES-D, to reduce measurement error. With the aim of improving model fit, modification indices were inspected, and cross-loadings or residual correlations between individual items were added wherever this was also theoretically sound. Weighted least square means and variance (WLSMV) adjusted estimators were chosen in light of the individual items being measured on both nominal and ordinal scales. Factor scores were then created and standardized into *z*-scores (mean = 0, standard deviation = 1) for use as predictors in further analyses. In case of missing values for individual items, factor scores were estimated based on all other available information.

Cox proportional hazard regression

To study associations between the social relationship constructs identified by factor analysis and incident dementia (research question 2), Cox-proportional hazard regression analyses (survival analysis) were conducted. More specifically, factor *z*-scores generated by the CFA were used as main predictors in the survival analyses, resulting in hazard ratios (HRs) and their 95% confidence intervals (CI's). Incident dementia up to Wave 9 was regarded as failure event, and cases were recorded at every wave. Survival time was defined as period from the start of the observation period (i.e., the Wave 2 interview) until the time dementia was reported or until censoring (i.e., the last available interview). The midpoint between the previous and last available Wave was chosen as date of diagnosis. Covariates were added incrementally, starting with a minimally (age and gender) adjusted model (Model 1), with additional adjustments for education (Model 2), wealth (Model 3), and cardiovascular risk factors (hypertension, coronary heart disease, and diabetes; Model 4). The fully adjusted model (Model 4) thus included all socio-demographic and cardiovascular risk factors.

The proportional hazard assumption was assessed both numerically using Schoenfeld residuals (Schoenfeld, 1982) and through visual inspection of clog–log plots. As ELSA participants could also be selected from the same household, we additionally adjusted for household clusters using a sandwich estimator. Furthermore, baseline cross-sectional weights were used to reduce selection bias by back-weighting estimates from the analytical sample to the full ELSA sample. The threshold level for statistical significance was chosen at $p \leqslant 0.05$ using two-sided tests. Survival analyses were conducted in Stata (StataCorp, 2021; version 17).

Structural equation modeling (mediation analyses)

Next, we examined whether depressive symptoms may explain the association between social relationship factors and incident dementia (research question 3). First, standardized factor scores of the depression factor as derived from CFA were added to Model 4 of the survival analyses as continuous variable, and changes in HRs and their *p*-values examined. Whenever (partial) mediation was suggested in these additional survival analyses, structural equation modeling was used to decompose associations into total, direct, and indirect (depression-mediated) associations. In these mediation analyses, we controlled for the same covariates as in Model 4 of the survival analyses. The percentage of effect mediation was calculated by dividing the total indirect effect estimates by those of the total effect. Structural equation modeling was conducted in Mplus (Muthén & Muthén, 2017).

Assessing the possibility of reverse causation

The possibility of reverse causation (research question 4) was assessed in three ways. First, we added a composite score of baseline cognition as an additional covariate to Model 4 of the survival analyses. This entailed averaging *z*-scores of tests of memory (delayed recall of a word list), semantic fluency (animal naming), and temporal orientation. Next, we excluded people who developed dementia in the first 24 months after baseline. This step was subsequently repeated for dementia cases of the first 48 months. Finally, the analytical sample was stratified based on follow-up times ($\leqslant$5 years v. >5 years), and the main analyses were repeated for each follow-up stratum separately. In view of the resulting reduction in sample sizes and thus statistical power, only changes in HRs (rather than levels of significance) were assessed.

https://doi.org/10.1017/S0033291724001272 Published online by Cambridge University Press

Results

Sample characteristics

At baseline, participants were on average 66.3 years old (S.D. = 9.7) and 55.5% were female. Across a median follow-up time of 11.8 years (IQR = 5.9–13.9 years), 501 people developed dementia (67.9 cases per 10 000 person-years, 95%CI 62.2–74.1 cases). Compared to people who did not develop dementia during the study period, those who did were significantly older ($t = 19.1$; $p < 0.001$), more likely to be female ($\chi^2 = 6.3$; $p = 0.012$), had lower education ($\chi^2 = 49.0$; $p < 0.001$) and net-wealth ($\chi^2 = 25.1$; $p < 0.001$), more likely had hypertension ($\chi^2 = 21.4$; $p < 0.001$), coronary heart disease ($\chi^2 = 27.0$; $p < 0.001$) and diabetes ($\chi^2 = 11.5$; $p = 0.003$), and reported more depressive symptoms ($t = 5.0$; $p < 0.001$). Table 2 contains a summary of sample characteristics stratified by dementia status. An overview of incident dementia cases per study Wave is presented in online Supplementary Table 2.

Factor analysis of social relationship items (research question 1)

Step 1 – EFA. There were 58 people with missing information on all social relationship items and were thus excluded from the EFA. Zero-order correlations between individual items ranged from 0 to |.8|. After inspection of eigenvalues >1.0, as well as visual inspection of the scree plot for points of inflexion, the 6-, 7-, 8-, and 9-factor solutions were retained for further scrutiny. Online Supplementary Table 3 contains the fit indices of all examined solutions. One item (*'How often respondent feels in tune with the people around them'*) had a factor loading below the threshold of |.4| for all solutions and was not included in further analyses. A 7-factor solution showed adequate model fit ($RMSEA_{EFA} = 0.061$; $CFI_{EFA} = 0.93$; $TLI_{EFA} = 0.89$). Standardized factor loadings for this solution are presented in online Supplementary Table 4. Items relating to meeting up with/speaking on the phone with children and other families cross-loaded on factors reflecting positive experiences of support with the respective relationship type. For contact with friends, this was not the case, but all items pertaining to contact with friends loaded on a single factor. In the subsequent CFA, those items were loaded on only one factor specific to relationship type, in order to aid interpretability.

Step 2 – CFA. The structure of the resulting six-factor model was as follows; Three factors related to items on both frequency of contact and positive experiences of social support with children (factor called: $F_{children}$), other family (F_{family}), and friends ($F_{friends}$). Items relating to the engagement in social leisure activities loaded on a fourth factor ($F_{activity}$). Finally, items pertaining to negative experiences of social support (regardless of

Table 2. Baseline (Wave 2–2004/2005) characteristics of ELSA participants, stratified by incident dementia status up to Wave 9 (2018/2019)

	Overall sample	No dementia	Dementia	*p*-Value
N	7536	7035	501	
Age, mean (S.D.)	66.3 (9.7)	65.8 (9.5)	74.1 (8.7)	<0.001[a]
Sex[b]				
Male, *n* (%)	3353 (44.5)	3157 (44.9)	196 (39.1)	0.012[a]
Female, *n* (%)	4183 (55.5)	3878 (55.1)	305 (60.9)	
Education[b]				
Low, *n* (%)	2583 (34.3)	2345 (33.3)	238 (47.5)	<0.001[a]
Medium, *n* (%)	1647 (21.9)	1557 (22.1)	90 (17.9)	
High, *n* (%)	2788 (37.0)	2656 (37.8)	132 (26.4)	
Missing, *n* (%)	518 (6.9)	477 (6.8)	41 (8.2)	
Wealth tertile[b]				
Low, *n* (%)	2384 (31.6)	2177 (40.0)	207 (41.3)	<0.001[a]
Medium, *n* (%)	2639 (35.0)	2475 (35.2)	164 (32.7)	
High, *n* (%)	2513 (33.4)	2383 (33.9)	130 (26.0)	
Missing, *n* (%)	N/A	N/A	N/A	
Hypertension, *n* (%)[b]	3026 (40.2)	2772 (39.5)	247 (49.9)	<0.001[a]
Missing, *n* (%)	124 (1.7)	116 (1.7)	8 (1.6)	
Coronary heart disease, *n* (%)[b]	923 (12.5)	825 (11.7)	98 (19.6)	<0.001[a]
Missing, *n* (%)	383 (5.1)	357 (5.1)	26 (5.2)	
Diabetes, *n*	332 (4.4)	301 (4.3)	31 (6.2)	0.003[a]
Missing, *n* (%)	457 (6.1)	413 (5.6)	44 (8.9)	
Depressive symptoms, mean (S.D.)	1.6 (0.02)	1.5 (0.02)	2.0 (0.10)	<0.001[a]
Missing, *n* (%)	122 (1.6)	104 (1.5)	18 (3.6)	

[a]Statistically significant ($p \leqslant 0.05$).
[b]Due to rounding, percentages may not add up to 100.

https://doi.org/10.1017/S0033291724001272 Published online by Cambridge University Press

relationship type) and feelings of loneliness loaded on factors $F_{neg.exp.}$ and $F_{loneliness}$, respectively. The model fit of this solution was suboptimal (RMSEA = 0.10; CFI = 0.62; TLI = 0.60). Model modification indices suggested the addition of cross-loadings between items relating to contact frequency between relationship types, as well as between contact frequency and social activity items, incorporation of which significantly improved model fit (RMSEA = 0.04; CFI = 0.93; TLI = 0.92). Depression was then included as additional latent factor using all items of the CES-D ($F_{depression}$). The item '*Whether respondent felt lonely much of the time during the past week*' was cross-loaded on both $F_{loneliness}$ and $F_{depression}$. This final 7-factor (six social factors plus $F_{depression}$) solution showed good fit (RMSEA = 0.04; CFI = 0.93; TLI = 0.92). Figure 1 contains a simplified visual depiction of the factor structure derived from CFA. Subsequent analyses involving $F_{children}$, F_{family} and $F_{friends}$ were restricted to those reporting to have children ($n = 5881$), other family ($n = 6285$), and friends ($n = 6464$), respectively.

Associations between social relationship constructs and incident dementia (research question 2)

Multivariable Cox regression then studied the relation between the social relationship factors and incident dementia (Table 3). Higher z-scores of $F_{children}$ were associated with lower dementia risk (Model 4: HR = 0.88; 95%CI 0.79–0.98; $p = 0.021$), as were higher z-scores of $F_{activity}$ (Model 4: HR = 0.84; 95%CI 0.74–0.94; $p < 0.001$). In contrast, higher z-scores of $F_{loneliness}$ (Model 4; HR = 1.13; 95%CI 1.03–1.25; $p = 0.011$) and $F_{neg.exp.}$ (Model 4: HR = 1.10; 95%CI 1.00–1.20; $p = 0.047$) were associated with higher dementia risk. Neither of the other two social factors significantly predicted dementia risk in Model 4.

Mediation by depressive symptoms (research question 3)

Structural equation modeling identified significant indirect effects (mediation) by depressive symptoms ($F_{depression}$) for $F_{children}$ (40.7% mediation; HR = 0.82; $p = 0.006$), $F_{activity}$ (50.7% mediation; HR = 0.84; $p = 0.010$), $F_{neg.exp.}$ (47.6% mediation; HR = 1.16; $p = 0.009$), and $F_{loneliness}$ (78.8% mediation; HR = 1.49; $p = 0.016$; online Supplementary Figures 1-4).

In the opposite direction (i.e., using the individual factor scores as mediators), no significant indirect (mediated) effects of depressive symptoms via $F_{children}$, $F_{activity}$, $F_{neg.exp.}$, or $F_{loneliness}$ on incident dementia were observed (results not shown).

The possibility of reverse causation (research question 4)

The results observed in the Cox proportional hazard regression remained virtually unchanged after adding baseline cognition and excluding incident dementia cases of the first 24 and 48 months. When assessing those with ⩽5 and >5 years of follow-up separately, associations remained directionally similar, though significant only for those with >5 years of follow-up for z-scores of $F_{activity}$. In the analyses only including those with ⩽5 years of follow-up, associations were not statistically significant and attenuated for z-scores of $F_{children}$ and $F_{loneliness}$. For z-scores of $F_{activity}$, an inverse association was found (HR = 1.13) in those with ⩽5 years of follow-up. Detailed results of analyses for assessing the possibility of reverse causation can be found in Table 4.

Discussion

In this study, we examined the presence of different social relationship constructs and their associations with incident dementia across 15 years of follow-up in the general English population. Factor analysis suggested six distinct social relationship factors. Higher scores on factors pertaining to the frequency and the quality of contact with children, social leisure activity engagement, as well as lower scores on factors concerning negative experiences of social support and loneliness were associated with lower dementia risk. These associations were independent of age, gender, education, wealth, and cardiovascular risk factors. Furthermore, for all four factors, associations were partly mediated by depressive symptoms. In additional analyses aiming to assess the possibility of reverse causation, associations remained largely unchanged.

Social relationship factors and dementia risk

The finding that the quality and quantity of contact with the respondent's children (as opposed to other family and friends) was predictive for incident dementia aligns with some studies suggesting the potential protective role of some structural aspects of intergenerational contact for cognition and dementia risk (Fratiglioni, Wang, Ericsson, Maytan, & Winblad, 2000; Meister & Zahodne, 2022; Zahodne, Ajrouch, Sharifian, & Antonucci, 2019). Other studies also found associations between contact with family and/or friends and cognitive decline and dementia (Meister & Zahodne, 2022; Sharifian, Kraal, Zaheed, Sol, & Zahodne, 2020; Sommerlad, Sabia, Singh-Manoux, Lewis, & Livingston, 2019; Zahodne et al., 2019). While directionally similar, these associations were not significant in the current study. In general, a disaggregation of social relationship types, as suggested by our factor analysis and in line with the social convoy model (Antonucci, Ajrouch, & Birditt, 2014), may be useful in light of the different functions and resources offered by different people in someone's social network (Antonucci et al., 2014; Gurung, Taylor, & Seeman, 2003; Meister & Zahodne, 2022; Sharifian et al., 2021).

The finding that more social leisure activity engagement was associated with lower dementia risk aligns with a growing body of literature suggesting its potential role in curbing age-related cognitive decline and lowering dementia risk (Duffner et al., 2022; Su et al., 2022). Likewise, the finding that lower levels of negative experiences of social support and loneliness were associated with lower dementia risk, is in line with some studies (Khondoker et al., 2017; Kuiper et al., 2015). However, evidence for the role of loneliness as a risk factor for dementia is generally more mixed. This may be due to heterogeneity in study populations and the operationalization of loneliness (Kuiper et al., 2015; Penninkilampi, Casey, Singh, & Brodaty, 2018; Qiao et al., 2022; Samtani et al., 2022).

Notably, we found little evidence for reverse causation. A large prospective study with modestly longer follow-up times of up to 20 years suggested that reverse causation might explain the association between social leisure activity engagement and dementia (Floud et al., 2021). In that study, authors found weaker associations with longer follow-up duration, which was not the case in ELSA. It was, however, conducted in a women-only cohort, which may hamper comparability with the current study. Likewise, while Floud et al. (2021) did include a range of activities with a social component (e.g., attending groups for art, craft, or

https://doi.org/10.1017/S0033291724001272 Published online by Cambridge University Press

https://doi.org/10.1017/S0033291724001272 Published online by Cambridge University Press

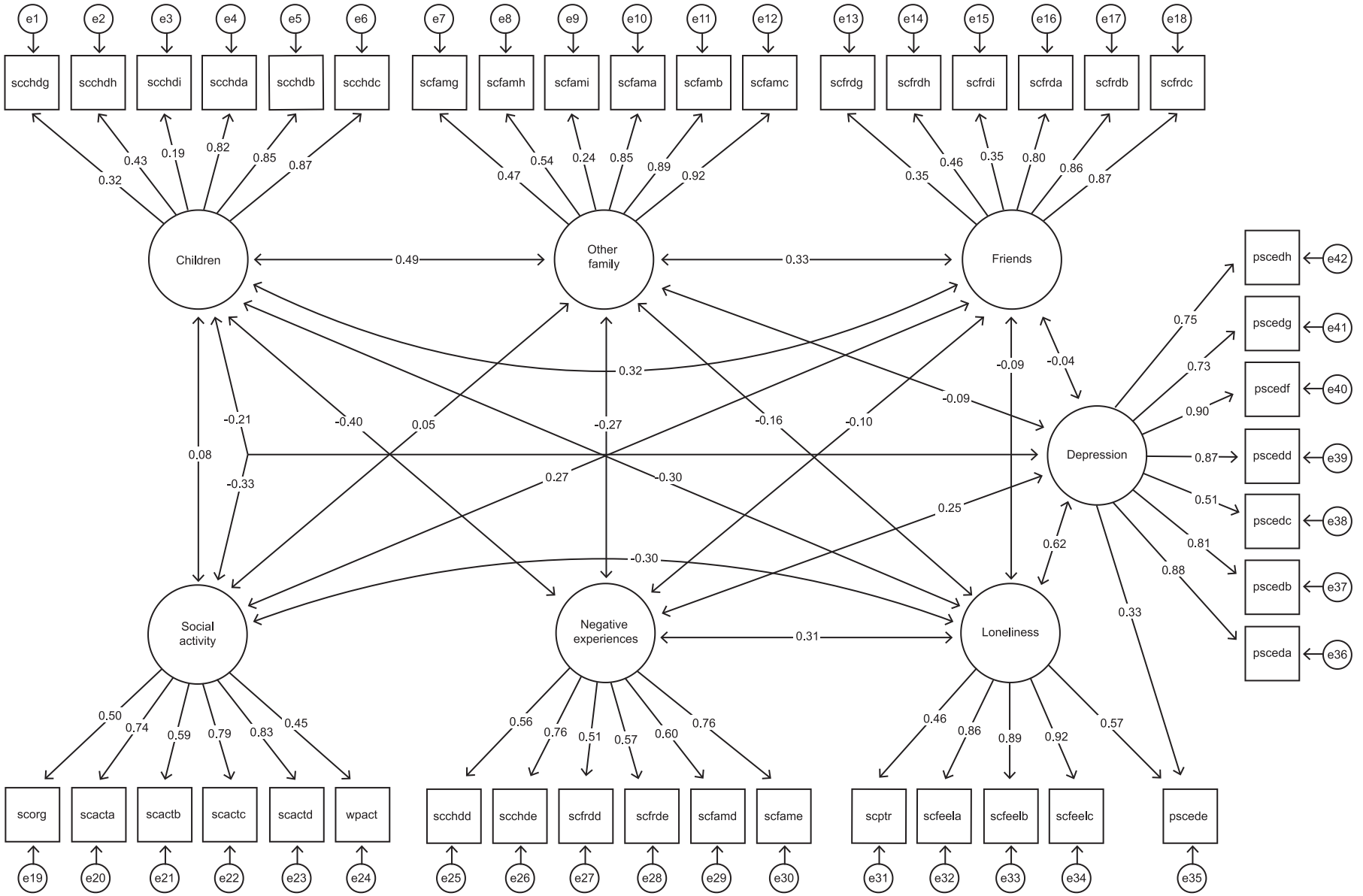

Figure 1. Simplified diagram of factor structure derived from confirmatory factor analysis of items pertaining to social relationship factors and depression in ELSA. Squares represent measured variables and circles indicate latent variables. Single headed arrows indicate variables loading on another variable. Double-headed arrows represent statistically significant correlations. All factor loadings are standardized. Note: for reasons of visibility, correlations between residuals of individual items are not shown.

Table 3. Results of Cox proportional hazard regression based on factor scores of social constructs

	$F_{children}$[a]		F_{family}[b]		$F_{friends}$[c]		$F_{activity}$		$F_{neg\_exp.}$		$F_{loneliness}$	
	N	HR (95%CI)	N	HR (95%CI)	N	HR (95%CI)	N	HR (95%CI)	N	HR (95%CI)	N	HR (95%CI)
Model 1	5881	**0.87 (0.79–0.96)**[d]	6285	0.94 (0.86–1.04)	6464	0.95 (0.87–1.04)	7531	**0.77 (0.70–0.84)**[d]	7531	**1.14 (1.05–1.25)**[d]	7531	**1.24 (1.14–1.35)**[d]
Model 2	5455	**0.88 (0.79–0.97)**[e]	5835	0.95 (0.85–1.05)	6008	0.97 (0.89–1.07)	7013	**0.81 (0.73–0.90)**[d]	7013	**1.12 (1.02–1.22)**[e]	7013	**1.20 (1.09–1.31)**[d]
Model 3	5455	**0.88 (0.80–0.98)**[e]	5835	0.95 (0.86–1.05)	6008	0.98 (0.89–1.07)	7013	**0.82 (0.74–0.92)**[d]	6998	**1.11 (1.01–1.21)**[e]	7013	**1.18 (1.08–1.29)**[d]
Model 4	4981	**0.88 (0.79–0.98)**[e]	5329	0.94 (0.84–1.06)	5482	0.98 (0.89–1.08)	6356	**0.84 (0.74–0.94)**[d]	6356	**1.10 (1.00–1.20)**[e]	6356	**1.13 (1.03–1.25)**[e]
Model 5	4942	0.93 (0.83–1.04)	5292	0.97 (0.87–1.08)	5442	1.00 (0.91–1.10)	6258	0.90 (0.79–1.02)	6258	1.03 (0.93–1.14)	6342	0.96 (0.84–1.11)

CI, confidence interval; HR, hazard ratio.
[a]Sample restricted to those reporting to have children;
[b]Sample restricted to those reporting to have other family;
[c]Sample restricted to those reporting to have friends;
[d]$p \leqslant 0.01$;
[e]$p \leqslant 0.05$.
Model 1 = age + gender; Model 2 = model 1 + education; Model 3 = model 2 + net-wealth; Model 4 (main model) = model 3 + heart disease, hypertension and diabetes; Model 5 = model 4 + $F_{depression}$.

music), the only overlap with activities included in the current study was voluntary work.

Another study assessed reverse causation in the association between trajectories of loneliness and cognition using cross-legged panel models. While cognition predicted changes in loneliness, there was no evidence for the pathway being the other way around (Okely, Deary, & Gutchess, 2019). However, in the current study, adding baseline cognition as a covariate or excluding incident dementia cases of the first 24 and 48 months did not weaken associations between the social relationship factors and incident dementia. Also splitting follow-up time, while lowering the number of incident cases per stratum and thus reducing statistical power, was not suggestive of reverse causation. Yet, in light of the observational nature of the current study, the possibility of reverse causation can never be entirely disregarded. It must also be noted that explanations are not mutually exclusive but that a bi-directional relationship might exist, in which poor social relationships increase dementia risk while impending dementia lowers social participation and contact frequency (Xiang et al., 2021).

Potential socioemotional and neurobiological pathways

The significant associations between the social relationship factors and dementia risk, as suggested by survival analyses, may align with the concept of cognitive reserve. This heuristic concept postulates that life experiences may lead to more flexibility in cognitive processes, which may help maintain mental functioning in light of neuropathology (Stern, 2002; Stern et al., 2018). In addition to a potential effect on cognition via such functional mechanisms, different aspects of social relationships may also be directly related to brain structure. More specifically, larger social network size, more social support, lower levels of loneliness, and more social activity engagement have been positively associated with brain volumes and microstructural integrity, also in brain areas implicated in cognitive aging (Duffner et al., 2023).

This study also explored a potential indirect socioemotional pathway by which social relationship factors may affect dementia risk, in addition to the postulated direct effects on brain structure and function. Specifically, mediation analyses showed that a significant proportion of the association between identified social relationship factors and dementia risk was explained by differences in depressive symptoms, ranging from 41% for contact with children to 79% for loneliness. While the role of social relationships in mood regulation, including the prevention and treatment of depression, has been recognized by the scientific community, this study is the first to structurally assess this in relation to long-term dementia risk (Campos-Paíno et al., 2023; Lee, Lee, & Yu, 2022). Social relationships serve as a source of instrumental, informational, and emotional support and may thus play a role in actively coping with psychological distress and depressive symptoms. Some studies proposed a potential 'social buffering' of the hypothalamic-pituitary-adrenocortical (HPA) axis, which is suggested to be especially responsive to psychological stressors (Hennessy, Kaiser, & Sachser, 2009). Long-term exposure to such stressors, in turn, has been associated with Alzheimer's disease pathology (Bisht, Sharma, & Tremblay, 2018). However, different types of chronic stressors (e.g., poverty) have also been identified as risk factors for depression itself (Chung et al., 2018; McDonald, Thompson, Perzow, Joos, & Wadsworth, 2020). In addition, depressed individuals also show a heightened vulnerability to psychological stressors in general, which may create a vicious cycle (Leonard, 2010). While some studies have

https://doi.org/10.1017/S0033291724001272 Published online by Cambridge University Press

Table 4. Analyses assessing the possibility of reverse causation

	Original model (HR)[a]	Adding baseline cognition (HR)	Excluding cases of <24 months (HR)[a]	Excluding cases of <48 months (HR)[a]	Splitting up FU-time (HR)[a]	
					⩽5 years	*>5years*
$F_{children}$[b]	**0.88**[c]	**0.87**[c]	**0.87**[c]	0.89	0.94	0.89
F_{family}[d]	0.94	0.92	0.92	0.91	1.15	0.93
$F_{friends}$[e]	0.97	0.96	0.97	0.96	1.11	0.97
$F_{activity}$	**0.84**[c]	**0.83**[c]	**0.83**[c]	**0.80**[c]	1.13	**0.80**[c]
$F_{neg.exp.}$	**1.10**[c]	**1.12**[c]	**1.11**[c]	1.07	1.16	1.08
$F_{loneliness}$	**1.13**[c]	**1.15**[c]	**1.14**[c]	**1.13**[c]	1.06	1.11

Abbreviations: HR, hazard ratio; FU, follow-up.
[a]Model 4;
[b]Sample restricted to those reporting to have children;
[c]Statistically significant ($p \leqslant 0.05$);
[d]Sample restricted to those reporting to have other family;
[e]Sample restricted to those reporting to have friends.

suggested a potential mediating role of social relationship factors in the association between broader life stressors and depression, their potential role in breaking such a vicious cycle, also in light of dementia risk, should be further examined in future studies (McDonald et al., 2020).

Implications and further directions

This study adds to the theoretical foundation concerning the interconnectedness of social relationship constructs and their potential pathways to dementia. In addition to this, it may also have practical implications. Our findings support the idea that dementia risk reduction programs might benefit from addressing broader socioemotional factors, such as feelings of loneliness as well as social activity engagement and intergenerational contact, in addition to a brain-healthy lifestyle in general. The stimulation of social interaction has also become a central element in ongoing multi-component lifestyle intervention trials, such as worldwide equivalents of the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (WW-FINGER; Kivipelto et al., 2013, 2020). The specific contribution of social relationship factors in such trials, however, should be subject to further research, as should be the identification of subpopulations that could benefit most from a more socially active lifestyle. Furthermore, social relationships are likely subject to change over time. To better capture such changes, studies with multiple measurement points over an extended period of time are necessary. Taking such a life-course perspective of social relationships may help identify possible 'windows of opportunity' for prevention.

Strengths and limitations

This study has several strengths, including a large cohort that is representative of the general English population and a long follow-up. Social relationship factors were derived from comprehensive factor analysis rather than face validity or single items, and putative mediation was tested in structural equation modeling. Yet, it also has some limitations. Firstly, most data used in the current study is based on self-report, which can be subject to social desirability and other sources of information bias (Althubaiti, 2016). This may also concern information about dementia status and, even though in the current study we resorted to a combination of self- and informant-report, the number of people with dementia within ELSA may still be underestimated.

Furthermore, due to missing values on some covariates, the sample in the Cox analyses was restricted to those with complete information on included variables. However, comparisons between those with and without missing information did not suggest the selection of a generally healthier sample. Notably, missing information on the main predictors could be restricted to those with missing values on all of the social relationship items included in the factor analysis ($n = 58$), as otherwise missing factor scores were imputed in factor analysis by means of maximum likelihood.

Next, model selection following EFA and CFA was, in part, based on known fit indices. The appropriateness of such scaled indices in models using WLSMV estimators has been questioned. More specifically, it has been proposed that they may be too liberal and likely to not identify model-data misfit, especially when data is of a categorical nature (Xia & Yang, 2019). Given the absence of viable alternatives, a factor analytical approach to studying social relationship constructs may still be superior to merely relying on face validity.

Lastly, the associations between factor scores and incident dementia might have been driven by variables not considered in the current analyses, such as mobility factors, occupational complexity, or parental socioeconomic status.

Conclusion

In the current study, the frequency and quality of social relationships were associated with lower dementia risk and may be suitable targets for dementia risk reduction initiatives in addition to social activity engagement. Mediation analyses suggested that these factors are partly associated with dementia risk via depressive symptoms. Additional analyses provided little evidence for reverse causation.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291724001272.

Data availability statement. ELSA data is freely accessible via the UK data service (https://beta.ukdataservice.ac.uk/datacatalogue/series/series?id=200011)

https://doi.org/10.1017/S0033291724001272 Published online by Cambridge University Press

Acknowledgements. We would like to thank the ELSA study participants.

Author contributions. Lukas A. Duffner: conceptualization and study design, data analysis, drafting the manuscript. Kay Deckers: conceptualization and study design, data analysis, critical revision of the manuscript. Dorina Cadar: critical revision of the manuscript. Marjolein de Vugt: conceptualization, critical revision of the manuscript. Sebastian Köhler: conceptualization and study design, data analysis, critical revision of the manuscript.

Funding statement. Lukas Duffner was supported by the Stichting Adriana van Rinsum-Ponsen and the Health Foundation Limburg.

Competing interests. The authors declare none.

References

Almeida-Meza, P., Steptoe, A., & Cadar, D. (2021). Is engagement in intellectual and social leisure activities protective against dementia risk? Evidence from the English longitudinal study of ageing. *Journal of Alzheimer's Disease*, *80*(2), 555–565. doi:10.3233/JAD-200952

Althubaiti, A. (2016). Information bias in health research: Definition, pitfalls, and adjustment methods. *Journal of Multidisciplinary Healthcare*, *9*, 211–217. https://doi.org/10.2147/JMDH.S104807

Amieva, H., Stoykova, R., Matharan, F., Helmer, C., Antonucci, T. C., & Dartigues, J. F. (2010). What aspects of social network are protective for dementia? Not the quantity but the quality of social interactions is protective up to 15 years later. *Psychosomatic Medicine*, *72*(9), 905–911. https://doi.org/10.1097/PSY.0b013e3181f5e121

Antonucci, T. C., Ajrouch, K. J., & Birditt, K. S. (2014). The convoy model: Explaining social relations from a multidisciplinary perspective. *The Gerontologist*, *54*(1), 82–92. https://doi.org/10.1093/geront/gnt118

Bielak, A. A. M., & Gow, A. J. (2022). A decade later on how to "Use It" so we don't "lose It": An update on the unanswered questions about the influence of activity participation on cognitive performance in older age. *Gerontology*, *69*(3):336–355. doi:10.1159/000524666

Bisht, K., Sharma, K., & Tremblay, M. È. (2018). Chronic stress as a risk factor for Alzheimer's disease: Roles of microglia-mediated synaptic remodeling, inflammation, and oxidative stress. *Neurobiology of Stress*, *9*, 9–21. https://doi.org/10.1016/j.ynstr.2018.05.003

Campos-Paíno, H., Moreno-Peral, P., Gómez-Gómez, I., Conejo-Cerón, S., Galán, S., Reyes-Martín, S., … Bellón, J. Á. (2023). Effectiveness of social support-based interventions in preventing depression in people without clinical depression: A systematic review and meta-analysis of randomized controlled trials. *International Journal of Social Psychiatry*, *69*(2), 253–266. https://doi.org/10.1177/00207640221134232

Chung, R. Y.-N., Chung, G. K.-K., Gordon, D., Wong, S. Y.-S., Chan, D., Lau, M. K.-W., … Wong, H. (2018). Deprivation is associated with worse physical and mental health beyond income poverty: A population-based household survey among Chinese adults. *Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, *27*(8), 2127–2135. https://doi.org/10.1007/s11136-018-1863-y

Deckers, K., Van Boxtel, M. P. J., Schiepers, O. J. G., De Vugt, M., Sánchez, J. L. M., Anstey, K. J., … Köhler, S. (2015). Target risk factors for dementia prevention: A systematic review and Delphi consensus study on the evidence from observational studies. *International Journal of Geriatric Psychiatry*, *30*(3), 234–246. https://doi.org/10.1002/gps.4245

Duffner, L. A., Deckers, K., Cadar, D., Steptoe, A., de Vugt, M., & Köhler, S. (2022). The role of cognitive and social leisure activities in dementia risk: Assessing longitudinal associations of modifiable and non-modifiable risk factors. *Epidemiology and Psychiatric Sciences*, *31*, e5. https://doi.org/10.1017/s204579602100069x

Duffner, L. A., DeJong, N. R., Jansen, J. F. A., Backes, W., de Vugt, M., & Köhler, S. (2023). Associations between social health factors, cognitive activity and neural markers for brain health – a systematic literature review and meta-analysis. *Ageing Research Reviews*. *89*, 101986. https://doi.org/10.1016/j.arr.2023.101986

Fancourt, D., Steptoe, A., & Cadar, D. (2020). Community engagement and dementia risk: Time-to-event analyses from a national cohort study. *Journal of Epidemiology and Community Health*, *74*(1), 71–77. https://doi.org/10.1136/jech-2019-213029

Floud, S., Balkwill, A., Sweetland, S., Brown, A., Reus, E. M., Hofman, A., … Beral, V. (2021). Cognitive and social activities and long-term dementia risk: The prospective UK Million Women Study. *The Lancet Public Health*, *6*(2), e116–e123. https://doi.org/10.1016/S2468-2667(20)30284-X

Fratiglioni, L., Wang, H. X., Ericsson, K., Maytan, M., & Winblad, B. (2000). Influence of social network on occurrence of dementia: A community-based longitudinal study. *The Lancet*, *355*(9212), 1315–1319. https://doi.org/10.1016/S0140-6736(00)02113-9

Gurung, R. A. R., Taylor, S. E., & Seeman, T. E. (2003). Accounting for changes in social support among married older adults: Insights from the MacArthur Studies of Successful Aging. *Psychology and Aging*, *18*(3), 487–496. https://doi.org/10.1037/0882-7974.18.3.487

Hennessy, M. B., Kaiser, S., & Sachser, N. (2009). Social buffering of the stress response: Diversity, mechanisms, and functions. *Frontiers in Neuroendocrinology*, *30*(4), 470–482. https://doi.org/10.1016/j.yfrne.2009.06.001

Hooper, D., Coughlan, J., Mullen, M. R., Mullen, J., Hooper, D., Coughlan, J., & Mullen, M. R. (2008). Structural equation modelling : Guidelines for determining model fit structural equation modelling : Guidelines for determining model fit. *The Electronic Journal of Business Research Methods*, *6*(1), 53–60.

John, A., Patel, U., Rusted, J., Richards, M., & Gaysina, D. (2019). Affective problems and decline in cognitive state in older adults: A systematic review and meta-analysis. *Psychological Medicine*, *49*(3), 353–365. https://doi.org/10.1017/S0033291718001137

Jorm, A. F. (1994). A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): Development and cross-validation. *Psychological Medicine*, *24*(1), 145–153. https://doi.org/10.1017/s003329170002691x

Khondoker, M., Rafnsson, S. B., Morris, S., Orrell, M., & Steptoe, A. (2017). Positive and negative experiences of social support and risk of dementia in later life: An investigation using the English longitudinal study of ageing. *Journal of Alzheimer's Disease*, *58*(1), 99–108. https://doi.org/10.3233/JAD-161160

Kivipelto, M., Mangialasche, F., Snyder, H. M., Allegri, R., Andrieu, S., Arai, H., … Carrillo, M. C. (2020). World-Wide FINGERS Network: A global approach to risk reduction and prevention of dementia. *Alzheimer's and Dementia*, *16*(7), 1078–1094. https://doi.org/10.1002/alz.12123

Kivipelto, M., Solomon, A., Ahtiluoto, S., Ngandu, T., Lehtisalo, J., Antikainen, R., … Soininen, H. (2013). The Finnish geriatric intervention study to prevent cognitive impairment and disability (FINGER): Study design and progress. *Alzheimer's and Dementia*, *9*(6), 657–665. https://doi.org/10.1016/j.jalz.2012.09.012

Kuiper, J. S., Zuidersma, M., Oude Voshaar, R. C., Zuidema, S. U., van den Heuvel, E. R., Stolk, R. P., & Smidt, N. (2015). Social relationships and risk of dementia: A systematic review and meta-analysis of longitudinal cohort studies. *Ageing Research Reviews*, *22*, 39–57. https://doi.org/10.1016/j.arr.2015.04.006

Lee, S. H., Lee, H., & Yu, S. (2022). Effectiveness of social support for community-dwelling elderly with depression: A systematic review and meta-analysis. Healthcare (Basel, *Switzerland*) *10* (9), 1598. https://doi.org/10.3390/healthcare10091598

Leonard, B. E. (2010). The concept of depression as a dysfunction of the immune system. *Current Immunology Reviews*, *6*(3), 205–212. https://doi.org/10.2174/157339510791823835

Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., … Cooper, C. (2020). Dementia prevention, intervention, and care: 2020 report of the *Lancet* Commission. *Lancet (London, England)*, *396*(10248), 413–446. https://doi.org/10.1016/S0140-6736(20)30367-6

McDonald, A., Thompson, A. J., Perzow, S. E. D., Joos, C., & Wadsworth, M. E. (2020). The protective roles of ethnic identity, social support, and coping on depression in low-income parents: A test of the adaptation to poverty-related stress model. *Journal of Consulting and Clinical Psychology*, *88*(6), 504–515. https://doi.org/10.1037/ccp0000477

Meister, L. M., & Zahodne, L. B. (2022). Associations between social network components and cognitive domains in older adults. *Psychology and Aging*, *37*(5), 591–603. https://doi.org/10.1037/pag0000672

Muthén, L. K., & Muthén, B. O. (2017). *Mplus user's guide* (8th ed.). Los Angeles, CA: Muthén & Muthén.

Nichols, E., Steinmetz, J. D., Vollset, S. E., Fukutaki, K., Chalek, J., Abd-Allah, F., & …Vos, T. (2022). Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: An analysis for the Global Burden of Disease Study 2019. *The Lancet Public Health*, *7*(2), e105–e125. https://doi.org/10.1016/S2468-2667(21)00249-8

Okely, J. A., Deary, I. J., & Gutchess, A. (2019). Longitudinal associations between loneliness and cognitive ability in the lothian birth cohort 1936. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *74*(8), 1376–1386. https://doi.org/10.1093/geronb/gby086

Penninkilampi, R., Casey, A. N., Singh, M. F., & Brodaty, H. (2018). The association between social engagement, loneliness, and risk of dementia: A systematic review and meta-analysis. *Journal of Alzheimer's Disease*, *66*(4), 1619–1633. https://doi.org/10.3233/JAD-180439

Peterson, R. A. (2000). A meta-analysis of variance accounted for and factor loadings in exploratory factor analysis. *Marketing Letters*, *11*(3), 261–275. https://doi.org/10.1023/A:1008191211004

Qiao, L., Wang, G., Tang, Z., Zhou, S., Min, J., Yin, M., & Li, M. (2022). Association between loneliness and dementia risk: A systematic review and meta-analysis of cohort studies. *Frontiers in Human Neuroscience*, *16* (December), 1–8. https://doi.org/10.3389/fnhum.2022.899814

Quinn, T. J., Fearon, P., Noel-Storr, A. H., Young, C., McShane, R., & Stott, D. J. (2021). Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the detection of dementia within community dwelling populations. *The Cochrane Database of Systematic Reviews*, *7*(7), CD010079. https://doi.org/10.1002/14651858.CD010079.pub3

Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*(3), 385–401. https://doi.org/10.1177/014662167700100306

Rafnsson, S. B., Orrell, M., D'Orsi, E., Hogervorst, E., & Steptoe, A. (2020). Loneliness, social integration, and incident dementia over 6 years: Prospective findings from the English longitudinal study of ageing. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *75*(1), 114–124. https://doi.org/10.1093/geronb/gbx087

Samtani, S., Mahalingam, G., Lam, B. C. P., Lipnicki, D. M., Lima-Costa, M. F., Blay, S. L., & …Brodaty, H. (2022). Associations between social connections and cognition: A global collaborative individual participant data meta-analysis. *The Lancet Healthy Longevity*, *3*(11), e740–e753. https://doi.org/10.1016/S2666-7568(22)00199-4

Schoenfeld, D. (1982). Partial residuals for the proportional hazards regression model. *Biometrika*, *69*(1), 239–241. https://doi.org/10.2307/2335876

Sharifian, N., Kraal, A. Z., Zaheed, A. B., Sol, K., & Zahodne, L. B. (2020). Longitudinal associations between contact frequency with friends and with family, activity engagement, and cognitive functioning. *Journal of the International Neuropsychological Society*, *26*(8), 815–824. https://doi.org/10.1017/S1355617720000259

Sharifian, N., Manly, J. J., Zahodne, L. B., Morris, E. P., Schupf, N., Mayeux, R., & …Brickman, A. M. (2021). Social network characteristics moderate associations between cortical thickness and cognitive functioning in older adults. *Alzheimer's and Dementia 18*(2), 339–347. https://doi.org/10.1002/alz.12383

Sommerlad, A., Sabia, S., Singh-Manoux, A., Lewis, G., & Livingston, G. (2019). Association of social contact with dementia and cognition: 28-year follow-up of the Whitehall II cohort study. *PLoS Medicine*, *16*(8), 1–18. https://doi.org/10.1371/journal.pmed.1002862

StataCorp. (2021). *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LLC.

Steptoe, A., Breeze, E., Banks, J., & Nazroo, J. (2013a). Cohort profile: The English longitudinal study of ageing. *International Journal of Epidemiology*, *42*(6), 1640–1648. https://doi.org/10.1093/ije/dys168

Steptoe, A., Shankar, A., Demakakos, P., & Wardle, J. (2013b). Social isolation, loneliness, and all-cause mortality in older men and women. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(15), 5797–5801. https://doi.org/10.1073/pnas.1219686110

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society : JINS*, *8*(3), 448–460.

Stern, Y., Arenaza-Urquijo, E. M., Bartrés-Faz, D., Belleville, S., Cantilon, M., Chetelat, G., … Vuoksimaa, E. (2018). Whitepaper: Defining and investigating cognitive reserve, brain reserve, and brain maintenance. *Alzheimer's and Dementia*, *16*(9), 1305–1311. https://doi.org/10.1016/j.jalz.2018.07.219

Su, S., Shi, L., Zheng, Y., Sun, Y., Huang, X., Zhang, A., … Lu, L. (2022). Leisure activities and the risk of dementia. *Neurology*, *99*(15), e1651 LP-e1663. https://doi.org/10.1212/WNL.0000000000200929

Unger, T., Borghi, C., Charchar, F., Khan, N. A., Poulter, N. R., Prabhakaran, D., … Schutte, A. E. (2020). 2020 International society of hypertension global hypertension practice guidelines. *Journal of Hypertension*, *38*(6), 982–1004. https://doi.org/10.1097/HJH.0000000000002453

Whitworth, J. A. (2003). 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. *Journal of Hypertension 21*(11), 1983–1992. https://doi.org/10.1097/00004872-200311000-00002

World Health Organization. (2011). *Use of glycated haemoglobin (HbA1c) in diagnosis of diabetes mellitus: Abbreviated report of a WHO consultation*. Geneva, Switzerland: World Health Organization. https://apps.who.int/iris/handle/10665/70523

Xia, Y., & Yang, Y. (2019). RMSEA, CFI, and TLI in structural equation modeling with ordered categorical data: The story they tell depends on the estimation methods. *Behavior Research Methods*, *51*(1), 409–428. https://doi.org/10.3758/s13428-018-1055-2

Xiang, X., Lai, P. H. L., Bao, L., Sun, Y., Chen, J., Dunkle, R. E., & Maust, D. (2021). Dual trajectories of social isolation and dementia in older adults: A population-based longitudinal study. *Journal of Aging and Health*, *33*(1–2), 63–74. https://doi.org/10.1177/0898264320953693

Zahodne, L. B., Ajrouch, K. J., Sharifian, N., & Antonucci, T. C. (2019). Social relations and age-related change in memory. *Psychology and Aging*, *34*(6), 751–765. https://doi.org/10.1037/pag0000369

https://doi.org/10.1017/S0033291724001272 Published online by Cambridge University Press