TITLE PAGE

Loneliness, Social Isolation and Risk of Cardiovascular Disease in the English Longitudinal Study of Ageing

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**ABSTRACT**

**Background**: There is increasing evidence of an association between social relationships and morbidity in general, and CVD in particular. However, recent syntheses of the evidence raise two important questions: is it the perceived quality, or the more objective quantity of relationships, that matters most; and what are the implications of changes in relationships over time? In this study, we investigate the cumulative effects of loneliness and social isolation on incident cardiovascular disease (CVD).

**Design:** Secondary analysis of prospective follow-up data from the English Longitudinal Study of Ageing (ELSA).

**Methods:** To assess the association between social isolation or loneliness and incident CVD, lagged values of exposure to loneliness and isolation were treated as time-varying variables in discrete-time survival models controlling for potential confounders and established CVD risk factors.

**Results**: A total of 5,397 men and women aged 50+ were followed up for new fatal and non-fatal diagnoses of heart disease and stroke, between 2004 and 2010. Over a mean follow-up period of 5.4 years, 571 new cardiovascular events were recorded. We found that loneliness was associated with an increased risk of CVD (Odds Ratio: 1.27, 95% Confidence Interval: 1.01, 1.57). Social isolation, meanwhile, was not associated with disease incidence. There was no evidence of a cumulative effect over time of social relationships on CVD risk.

**Conclusions**: Loneliness is associated with an increased risk of developing CHD and stroke, independently of traditional CVD risk factors. Our findings suggest that primary prevention strategies targeting loneliness could help to prevent CVD.

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**KEYWORDS**

Cardiovascular disease; SOCIAL EPIDEMIOLOGY; LONGITUDINAL STUDIES

**INTRODUCTION**

There is growing evidence that adults who are socially isolated (i.e. who have few social contacts) or who feel lonely (i.e. unhappy about their social relationships) are at greater risk of cardiovascular disease (CVD). A recent meta-analysis of observational studies found that weaker social relationships were associated with a 29% increase in risk of incident heart disease, and a 32% increase in risk of stroke.1 Primary studies have highlighted three pathways through which social relationships can influence CVD risk: behavioural (e.g. smoking, physical inactivity), psychological (e.g. low self-esteem and self-efficacy) and biological (e.g. response to stress, allostatic load and cardiovascular reactivity).2

Social relationships change over time. Loneliness and social isolation may for example increase following widowhood, migration or a decline in functional capacity.3 Conversely, changes such as the birth of grandchildren can bring increased contact with children in later life, and research indicates that people continue to acquire new acquaintances and rekindle weakened ties in old age.4 Analyses that take into account the dynamic and multi-dimensional nature of social relationships are needed to inform the design of effective interventions. We therefore took advantage of the availability of repeated measures of loneliness and social isolation in a large-scale prospective cohort, the English Longitudinal Study of Ageing (ELSA),5 to investigate whether they were independently associated with an increased risk of incident CVD.

**METHODS**

**Participants**

ELSA is a population-based cohort study of adults aged fifty living in England, for which ethical approval was granted by the National Research Ethics Service. It began in 2002, with a sample of 11,391 individuals who in 1998, 1999 or 2000 took part in the Health Survey for England (HSE), an annual cross-sectional survey designed to monitor the population’s general health.6 For the HSE, participants were selected using a multi-stage stratified probability sampling design. First, UK postcode sectors stratified by health authority and the proportion of households in non-manual socio-economic groups were selected with probability proportional to their size. In a second stage, a fixed number of addresses were identified systematically from each postcode sector and households were selected for each address.7 A total of 31,051 households were sampled, of which 11,578 were eligible for ELSA (see Figure 1 for a summary of the sample definition process).

Comparison of the socio-demographic characteristics of the 11,391 people who eventually took part in ELSA’s first wave with national census data indicate that this sample was representative of the English population.5 Thereafter, members were surveyed every two years using computer-assisted personal interviews and self-completion questionnaires. Wave 5 was the last wave for which data on both fatal and non-fatal CVD events were available at the time of our analyses. We used wave 2 as the baseline for our study because this was the first wave at which core ELSA participants (i.e. excluding partners aged under 50) took part in a nurse visit where biomarkers pertinent to CVD risk – blood pressure and cholesterol – were measured. We excluded: participants diagnosed with a heart condition or stroke prior to wave 2, as we wanted to investigate first events; and individuals interviewed by proxy due to poor health or disability, since proxy questionnaires did not assess loneliness or isolation.

**Exposure: loneliness and social isolation**

Loneliness

We selected two instruments used in ELSA to capture loneliness feelings in waves 2,3 and 4 of ELSA: a direct single-item question, where participants were asked in person whether they agreed or not with one the statement ‘Much of the time during the past week, you felt lonely’;8 and the University of California, Los Angeles (UCLA) three-item Loneliness Scale, which covers the frequency and intensity of loneliness feelings and was administered via a self-completion questionnaire. Its three items are: How often do you feel you lack companionship? How often do you feel left out? How often do you feel isolated from others? For each question, participants could answer ‘hardly ever or never’ (score of 1), ‘some of the time’ (score of 2) or ‘often’ (score of 3). Total scores ranged from 3 to 9, with a higher score indicating greater levels of loneliness. This scale has been validated and shown to be reliable among older adults.9

Because we were specifically interested in whether the frequency (rather than the intensity) of loneliness was associated with risk of CVD, we chose the direct single-item question for our main analyses. We coded loneliness to reflect cumulative exposure up until the event or censoring – i.e. reporting feeling frequently lonely at none, one or two waves was coded as 0,1 and 2. The 3-item UCLA was used in sensitivity analyses. In line with previous studies, we used a score of 6 as the cut-off to distinguish between more and less lonely participants.10, 11

Social isolation

We adapted the index of social isolation developed by Shankar,10 assigning one point for each of the following 6 items: living alone; less than monthly face-to-face, telephone or written/e-mail contact with children outside the household; less than monthly contact with other relatives outside the household; less than monthly contact with friends; not participating in any organizations, religious groups, or committees; and not currently employed. Our rationale for adapting the Shankar index was that the former does not capture contact with relatives other than partners or spouse living at home, and nor does it tap into the potential network of colleagues one might access when in employment. Scores on our index ranged from 0 to 6, with higher scores indicating greater social isolation. Because we were specifically interested in whether the most isolated individuals were at increased risk of CVD, we dichotomized the index using 5 as the cut off score (i.e. those scoring 5 or 6 were classed as socially isolated). In our main analyses, we compared those who were classed as isolated in one or more waves (i.e. in waves 2, 3 or 4 of ELSA), with those who were never isolated. In sensitivity analyses, we first checked our findings against those obtained based on the measure developed by Shankar and colleagues; we then used the tool selected by Elovainio for analyses of the UK Biobank dataset.12

**Incident CVD**

Fatal CVD events were derived from the UK National Health Service Central Register, using ICD-9 codes 390-459 and ICD-10 codes I00-I99. Non-fatal events were reported by participants, according to whether they had been diagnosed with a heart condition or stroke since their last interview. New heart problem diagnoses included angina, heart attack, congestive heart failure, a heart murmur, an abnormal heart rhythm or any other heart trouble. Studies have found that respondents may be prone to mis-classify specific diagnoses of heart conditions and that self-reports have more validity when heart disease is defined more broadly.13, 14 Comparisons of estimates from clinically verified studies with self-reported incident stroke in ELSA’s sister study, the Health and Retirement Study, suggest that misreporting is non-systematic and that participant-reported events can be used to study stroke incidence and risk factors.15

**Covariates**

Items of the Framingham ten-year CVD risk score

To investigate whether loneliness and social isolation predicted CVD independently from the factors traditionally taken into account when assessing disease risk, we included the components of the Framingham score in our analyses. These include age, high-density lipoprotein (HDL) and total cholesterol, systolic blood pressure, treatment for hypertension, smoking and diabetes.16 At wave 2 of ELSA (the baseline wave for our study), blood samples were taken from participants with written consent who did not have a clotting or bleeding disorder and were not taking anti-coagulant drugs. Samples were assayed for total and HDL cholesterol, haemoglobin A1C and for fibrinogen and C-reactive protein at the Royal Victoria Infirmary in Newcastle-upon-Tyne, UK. Systolic blood pressure was measured three times using an Omron blood pressure monitor with the participant seated; the mean of the last two readings was used in our analysis. Participants were asked about their smoking status and whether they were taking any medication for high blood pressure. We defined prevalent diabetes mellitus based on reported doctor-diagnosed diabetes and/or use of diabetes medication, or a haemoglobin A1C level ≥6.5 %.17 Each variable was entered separately into our analytical models; in a sensitivity analysis, we checked whether our results changed when we substituted the individual items with the overall Framingham score predicting 10-year CVD risk, as used in clinical practice.

Total household wealth

In addition to the factors included in the Framingham score, we identified socioeconomic status as a potential confounder.18, 19 We used total household wealth quintiles, a robust indicator of socioeconomic circumstances and standard of living in ELSA which includes financial wealth, the value of any home and other property, the value of business assets, physical wealth such as artwork and jewelry and debt.20, 21

**Statistical analysis**

Associations between social relationship measures and CVD incidence were estimated with odds ratios and 95% confidence intervals computed in discrete-time survival analyses. Discrete time models were chosen because the exact time at which events occurred was unknown, and because such models easily accommodate time-varying variables that have not been measured continuously over time. Multinomial logit models allowed us to model non CVD-death as a competing risk.22 After running separate models for loneliness and isolation only (models A and B), we adjusted for potential confounders (model C, adjusting for household wealth quintile, age and gender), before adding in the rest of the Framingham score items (model D). All models satisfied the minimum requirement of 10 events per parameter. The proportional hazards assumption was checked by testing whether an interaction term between time and the independent variables was significant. In all models, the values used for loneliness and isolation were lagged values – i.e. the models sought to investigate whether the number of times a person reported feeling lonely or being isolated in the waves *prior* to CVD event assessment predicted the likelihood of event. Sensitivity analyses were run to gauge whether results changed when the Framingham score, UCLA Loneliness Scale, Shankar or Elovainio indices of social isolation were used.

We assessed missing data for all the variables in our analyses and used multiple imputation by chained equations with 25 replications, under the assumption that values were missing at random.23, 24 The imputation model included the event indicator, the Nelson-Aalen estimator, age, gender, total household wealth, HDL cholesterol, total cholesterol, systolic blood pressure, treatment for hypertension, smoking, diabetes, and loneliness and social isolation at each wave. We used Rubin's rules (1987) to pool the imputation estimates.23

All statistical analyses were conducted using Stata SE 14.2.25 and the significance level used was 5%.

**RESULTS**

**Study population**

Of the 11,391 core members who participated in the first wave of ELSA, 8,780 (77%) completed the main interview in wave 2. Eighty-one per cent (7,029) of those who were interviewed in person completed a questionnaire and took part in the nurse visit. After excluding the 1,482 people who reported a heart problem or stroke diagnosis prior to wave 2, and the 150 people who went on to be interviewed by proxy, a total of 5,397 individuals were eligible for our analyses (see Figure 1 for a summary of the sample selection process).

Figure 1 here.

The percentage of missing values at baseline ranged from none for age and gender to 19% for HDL cholesterol. Taking into account patterns of missingness for the two social relationship variables across the six-year study period, only 62% of the study cohort would have been available for analysis under the traditional listwise deletion method. The distribution of imputed values closely fitted that of observed values and overall, results using listwise deletion were similar to those using multiple imputation. In this paper, we report imputed results; results from listwise deletion are provided in Supplement 1.

Participants’ descriptive characteristics are summarised in Tables 1 (baseline) and 2 (across waves).

Table 1 here.

Table 2 here.

**Loneliness, social isolation and incident CVD**

Over a mean follow-up period of 5.4 years, 571 first CVD events were recorded. Where participants reported a new stroke and heart condition in the same wave (n=10), these were only counted as one event in our analyses, since we were interested in first events only.

Associations between loneliness, social isolation and CVD incidence are displayed in Table 3.

Table 3 here.

Loneliness

In univariable analyses, reporting one instance of frequent loneliness was associated with an increased risk of incident CVD (Odds Ratio (OR) = 1.58, 95% Confidence Interval (CI): 1.23 to 2.04). There was no evidence of a cumulative association for loneliness over time: those who reported loneliness twice were not at greater risk of disease compared with those who reported loneliness once only (OR = 0.81, 95% CI: 0.50, 1.32). Nor were those who reported loneliness three times at higher risk compared to participants with one report only (OR: 1.16, 95% CI: 0.59, 2.30). In the multivariable model adjusting for age, gender, wealth and social isolation, the association between loneliness and CVD persisted (OR comparing one or more to no report of loneliness = 1.28, 95% CI: 1.02, 1.60). This association did not appear to be mediated by traditional CVD risk factors: when systolic blood pressure, total and HDL cholesterol, diabetes, hypertension medication and smoking status were added to the model, loneliness remained an independent predictor of risk (OR comparing one or more to no report of loneliness = 1.27, 95% CI: 1.01, 1.59). Sensitivity analyses based on the UCLA 3-item Scale suggested a similar magnitude of association between loneliness and increased risk of event (OR comparing once or more versus never lonely in model D: 1.21, 95% CI: 0.98, 1.49), and did not point to a cumulative association (see Supplement 2).

Social isolation

Social isolation was not identified as an independent predictor of CVD risk in our analyses (in model A, OR comparing at least one versus no instance of isolation: 1.25, 95% CI: 0.71, 2.20; in model D, OR = 0.75, 95% CI: 0.42,1.35). Sensitivity analyses based on the Shankar index suggested that isolation might predict CVD when no other variables were taken into account (crude OR: 1.20, 95% CI: 1.00, 1.44), but once age, gender, wealth and loneliness were introduced this association disappeared (adjusted OR: 0.93, 95% CI: 0.88, 1.30). Analyses using Elovainio’s index produced similar results to our main analyses (crude OR: 1.16, 95% CI: 0.89, 1.52; in the model adjusting for potential confounders and traditional CVD risk factors, OR = 0.79, 95% CI: 0.59, 1.06).

Associations between loneliness, isolation and disease incidence did not change when the items contributing to the Framingham score were replaced by CVD risk category – see Supplement 2 for the full set of results from the sensitivity analyses.

**DISCUSSION**

**Main findings and comparison with other work**

Our study found that reporting feeling lonely was associated with an increased risk of CVD: event rate was 27% higher among those who reported feeling lonely at least once over the six-year study period. The magnitude of this association is comparable to the influence of recognized psychosocial factors, including depression and anxiety.26, 27 There was no evidence of a cumulative association: reporting loneliness twice or three times was not associated with a stronger risk of CVD when compared with reporting one instance only.

To our knowledge, this is the first study to examine loneliness and social isolation simultaneously as time-dependent variables in relation to incident fatal and non-fatal cardiovascular risk. A previous Dutch study with multiple measures of loneliness had not reported clear evidence of an association between feeling lonely and cardiovascular mortality in older men (Hazard Ratio associated with being severely lonely: 1.18, 95% CI: 0.58, 2.39).28 The absence of a statistically significant effect is likely to have stemmed from the study’s relatively small sample size: 719 men in total, only 23 of which were classed as being ‘severely lonely’. Our study relied on a sample of over 5,000 individuals, surveyed every two years rather than every five in the Zutphen Elderly Study). Future studies with even shorter periods between data collection points will help to gauge the most appropriate timeframe for studying loneliness in relation to CVD incidence.

The association between loneliness and CVD incidence persisted when the main biological and behavioural CVD risk factors were controlled for, suggesting that the mechanisms at play may be more to do with psychological pathways (e.g. depression, anxiety, self-esteem) and/or other behaviours, including alcohol consumption and physical activity. Prospective longitudinal studies have identified loneliness as a risk factor for higher levels of depressive symptoms,29, 30 which in turn are associated with heightened risk of experiencing a CVD event.31, 32 Reviews of the literature have also highlighted loneliness as a risk factor for both higher alcohol consumption and lower physical activity.33, 34 Since health-related behaviours and psychological states can in turn influence loneliness, it is important to bear in mind that the latter may be a marker or ‘symptom’, rather than a cause, of the former. We know that psychosocial risk factors such as depression and anxiety are prevalent among people who have experienced a coronary event,28 and it may be that loneliness is a manifestation of subclinical symptoms related to CVD. Based on our data and analyses, we cannot assume that loneliness was a causal factor; further analyses will be needed to disentangle potential reverse causality and synergistic effects.

While univariate analyses suggested that social isolation might be linked to greater risk of CVD (with effect sizes ranging from 1.16 to 1.25 depending on the measure of isolation used), there was no evidence of an effect once loneliness and traditional risk factors were controlled for. This finding, along with our results relating to loneliness, suggests that the *quality* of relationships may be more important than quantity when assessing disease risk. Where people have chosen to have limited interaction with others, they may have developed resilience mechanisms and ways of countering the potentially detrimental consequences of isolation (e.g. by making sure that they continue to drive since they may not be able to rely on anyone else to do so for them, or by making sure that they regularly consult health care practitioners to prevent any worsening of their health). We know that interaction with others is not always beneficial, and wider networks may include negative social interactions such as conflict, demands and abuse, which have been linked to physiological processes including allostatic load35 and elevated hypothalamic-pituitary-adrenal axis responses.36

**Strengths and limitations**

Our study drew on the strengths of ELSA, a nationally representative cohort study of adults aged over 50 who provide robust demographic, social and biological data. This enabled us to incorporate into our analyses the risk factors routinely considered when assessing patients, to ensure that our analyses were relevant to clinical practice. The longitudinal design of the study allowed us to focus on the prospective association between social relationships and CVD, though we acknowledge that reverse causation – where deficiencies in social relationships are the result of subclinical disease – remains a possibility. Unfortunately, because not all variables were collected at each wave (e.g. the nurse visit was carried out every four years, i.e. in alternate waves), it was not possible for us to investigate whether, when treated as time-varying, the relationship between factors such as wealth or CVD risk factors and social relationships changed.

Since there is no consensus on which tools are most appropriate for assessing social relationships, we used multiple measures of loneliness and social isolation to test the robustness of our findings. We found no marked differences in results relating to either loneliness or social isolation, suggesting that a shorter index (as developed by Elovainio and colleagues, for example) could be sufficient to capture the implications of a person’s social network for health. Future studies comparing the overlap across measures, and their relationship with different outcomes, will help to clarify which tools might be most appropriate for use in epidemiological studies. Sensitivity analyses were also run using the Framingham score, which captures CVD risk over a ten-year period; the results obtained resembled those based on the baseline measures of cholesterol, diabetes, blood pressure, smoking status and hypertensive medication.

Non-fatal CVD events were self-reported by participants at every wave. While this is generally recognized as a relatively robust measure of outcomes such as myocardial infarction or stroke, it may be that participants omitted to, or incorrectly reported, certain events. The possibility that our results were affected by systematic misreporting cannot be excluded, and nor can we be certain that the month and year of diagnosis they provided was accurate.

Similarly to many other panel studies, attrition in ELSA is socio-economically graded and more severe among underprivileged individuals.5 Since lower socio-economic status is associated with weaker social relationships and CVD incidence, it may be that our analyses underestimate the effect of loneliness and social isolation. Participants lost to follow-up were more likely to report lower levels of education, be less wealthy, be older and report a limiting long-standing illness .5 Since socio-economic status, age and health are risk factors for loneliness and social isolation as well as CVD,10, 11, 18, 19, 37 it is possible that people lost to follow-up were more lonely or isolated, and at greater risk of CVD, compared with individuals who remained in the study. We also note that patients with prior events, and patients with otherwise poor health and disability, individuals on anticoagulant drugs, and those reporting clotting or bleeding disorders, were excluded from this study. These subjects could be more prone to isolation and at greater risk of CVD; their exclusion may explain that we found no association between social isolation and CVD incidence, and we cannot generalise our findings to these populations. Nor can we exclude confounding by other causes not included in our models. Many factors, such as depression and health-related behaviours, may be both confounders and on the causal pathway. Since survival analyses do not enable us to distinguish between these two effects, we restricted the variables in our models to the factors routinely assessed in practice. Our hypothesis was that loneliness and isolation could be markers of, if not causal factors for, disease risk. In common with other observational studies, we cannot infer causality from our data.

**Implications**

The finding that lonely individuals are at increased risk of CVD suggests that practitioners ought to take perceptions of social relationships into account when assessing patient risk. Identifying someone as lonely could help to flag up a person who may not be considered at risk of CVD according to traditional factors but whose likelihood of experiencing a CVD event is high nonetheless. More so than objective characteristics such as a the size, composition or diversity of a person’s social network, subjective perceptions of one’s relationships can provide insight into a person’s wellbeing; highlighting an individual’s loneliness could be the first step in preventing the development and worsening of other risk factors for CVD, including anxiety, depression and health-damaging behaviours such as smoking and drinking. The direct question included in the ELSA interview could be a useful tool for practitioners to identify people who would not otherwise be scored as being at risk of CVD with tools such as the Framingham score. Because individuals may not wish to publicly discuss negative feelings about the people in their lives, it will also be important to consider indirect measures such as the 3-item UCLA Scale9 or the de Jong Gierveld Loneliness Scale.38

From a public health perspective, our finding that repeated instances of loneliness, compared with only reporting loneliness once, were not associated with a higher risk of CVD suggests that it may be particularly difficult for secondary and tertiary prevention strategies to positively affect health outcomes. If loneliness reflects undiagnosed symptoms, then targeting people who already feel lonely may not reduce CVD risk. In the absence of evidence pointing to the health benefits of improvements in loneliness, primary prevention strategies could be a more promising way of tackling loneliness and its adverse health implications. To date, national initiatives including The Campaign to End Loneliness in the UK, Coalitie Erbij in the Netherlands and MONALISA in France have focused on strengthening the social relationships of people who already experience chronic loneliness. Existing initiatives led by the WHO and European Union (EU) to promote good health and wellbeing in later life, including Age-Friendly Cities and the EU’s ‘Healthy Ageing’ campaign, could in future broaden the agenda to primary prevention and incorporate a ‘loneliness’ component.

**STATEMENTS**

**Declaration of conflicting interests** ‘The author(s) declare(s) that there is no conflict of interest.

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**Author contribution** NKV developed the idea for the article and conducted the analyses under the supervision of MK, SG and BH. NKV wrote the first draft, with all authors contributing to critical revision of the manuscript for important intellectual content. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy. NKV is the guarantor.

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**TABLES AND FIGURES**

**Table 1** Sample Characteristics at Baseline

|  |  |
| --- | --- |
|  | Participants (n=5,397) |
| Variables used in main analyses |
| Age – mean (SD ), range | 65 (9), 52 to 90+ |
| Gender |
|  Female | 56% |
|  Male | 44% |
| Total household wealth (£ Pounds sterling) |
|  1 (lowest quintile) | Up to £62,900 |
|  2 | 62,920 to 159,760 |
|  3 | 159900 to 236,901 |
|  4 | 236,923 to 383,000 |
|  5 (highest quintile) | 383,450 to 9,297,227 |
| Framingham CVD risk score components |
|  Systolic blood pressure (mmHg) –  mean (SD), range | 135 (19), 80 to 259 |
|  Treatment for hypertension |
|  Yes | 13% |
|  No | 87% |
|  Smoking status |
|  Current smoker | 14% |
|  Not currently smoking | 86% |
|  Diabetes status |
|  Diabetic | 8% |
|  Not diabetic | 92% |
|  HDL cholesterol (mmHg) – mean  (SD), range | 60 (15), 19 to 139 |
|  Total cholesterol (mmHg) – mean  (SD), range | 234 (45), 81 to 476 |
| Variable used in sensitivity analyses |
| Framingham CVD 10-year risk score category |
|  Low (i.e. score below 10%) | 23% |
|  Medium (i.e. score 10 to 20%) | 38% |
|  High (i.e. score over 20%) |  38%\*\* |

\* Note that all ages over 90 are coded as 90 in ELSA.

\*\* Percentages do not add up  to 100 due to rounding.

**Table 2** Frequency of Loneliness and Social Isolation Across Waves

|  |  |  |  |
| --- | --- | --- | --- |
|

|  |  |
| --- | --- |
|  | Participants (n=5,397) |
| Variables used in main analyses Full-case data Imputed values\* |

Loneliness – according to single direct question  |
|  Not lonely at any wave | 80%  | 79% |
|  Once lonely during follow-up | 11% |
|  Twice lonely | 6% |
|  Thrice lonely | 4% |
| Social isolation – according to our Index of Social Contacts |
|  Not isolated at any wave | 97% | 96%  |
|  Once isolated | 2% | 3% |
|  Twice isolated | 1% |
|  Thrice isolated |  1%\*\* |
| Variables used in sensitivity analyses |
| Loneliness – measured with the UCLA 3-item Scale |
|  Not lonely at any wave | 69% |
|  Once lonely during follow-up | 14% |
|  Twice lonely | 9% |
|  Thrice lonely | 8% |
| Social isolation – according to index developed by Shankar and colleagues |
| Not isolated at any wave | 52% |
|  Once isolated | 16% |
|  Twice isolated | 12% |
|  Thrice isolated | 20% |
| Social isolation – according to index developed by Elovainio and colleagues |
|  Not isolated at any wave | 83% |
|  Once isolated | 9% |
|  Twice isolated | 5% |
|  Thrice isolated | 5% |

\* Where full-case and imputed values are the same, columns have been merged to avoid duplication.

\*\* Percentages do not add up to 100 due to rounding.

**Table 3** Association between Loneliness, Social Isolation and Cardiovascular Disease Incidence in ELSA in Uni- and Multi-variable Discrete-time Survival Analyses

|  |  |  |  |
| --- | --- | --- | --- |
|  | Univariable analyses (models A and B) | Estimates for model C | Estimates for model D |
| Explanatory variable(s) | Odds Ratio | 95% Confidence Interval | Odds Ratio | 95% Confidence Interval | Odds Ratio | 95% Confidence Interval |
| *Loneliness* |
|  Never | 1.00 |  | 1.00 |  | 1.00 |  |
|  Once (compared to never) | 1.58 | 1.23, 2.04 | 1.37 | 1.06, 1.78 | 1.36 | 1.05, 1.77 |
|  Twice (compared to once) | 0.81 | 0.50, 1.32 | 0.74 | 0.45, 1.22 | 0.74 | 0.45, 1.22 |
|  Thrice (compared to twice) | 1.44 | 0.67, 3.08 | 1.34 | 0.62, 2.90 | 1.33 | 0.62, 2.87 |
|  Comparing lonely at least once v. never | 1.52 | 1.23, 1.89 | 1.28 | 1.02, 1.60 | 1.27 | 1.01, 1.59 |
| *Social isolation* |
|  Never | 1.00 |  | 1.00 |  | 1.00 |  |
|  Comparing at least once | 1.25 | 0.71, 2.20 | 0.77 | 0.43, 1.38 | 0.75 | 0.42, 1.35 |
| *Age* (one year increase) | 1.06 | 1.05, 1.07 | 1.06 | 1.05, 1.07 | 1.06 | 1.05, 1.07 |
| *Gender* | 1.03 | 0.86, 1.22 | 1.12 | 0.94, 1.34 | 1.06 | 0.86, 1.29 |
| *Wealth* (quintiles) |  |  |  |  |  |  |
|  First (lowest) | 1.00 |  | 1.00 |  | 1.00 |  |
|  Second | 0.77 | 0.59, 1.00 | 0.84 | 0.64, 1.10 | 0.86 | 0.65, 1.12 |
|  Third  | 0.71 | 0.54, 0.93 | 0.81 | 0.62, 1.06 | 0.83 | 0.63, 1.10 |
|  Fourth | 0.71 | 0.54, 0.92 | 0.81 | 0.62, 1.06 | 0.84 | 0.64, 1.11 |
|  Fifth | 0.58 | 0.44, 0.76 | 0.72 | 0.54, 0.97 | 0.78 | 0.58, 1.04 |
| *Diabetes diagnosis* (yes v. no) | 1.26 | 0.92, 1.72 | Variable not included | 1.00 | 0.72, 1.39 |
| *Hypertensive medication* (yes v. no) | 1.56 | 1.24, 1.96 | Variable not included | 1.22 | 0.96, 1.54 |
| *Systolic blood pressure* (mean) | 1.01 | 1.01, 1.02 | Variable not included | 1.01 | 1.00, 1.01 |
| *Current smoking status* (yes v. no) | 0.96 | 0.74, 1.24 | Variable not included | 1.12 | 0.86, 1.47 |
| *Total cholesterol* (mean) | 1.00 | 1.00, 1.00 | Variable not included | 1.00 | 1.00, 1.00 |
| *HDL cholesterol* (mean) | 1.00 | 0.99, 1.00 | Variable not included | 1.00 | 1.00, 1.01 |
| *Framingham risk category*Low Medium High | 1.001.63 2.30 | 1.19, 2.241.69, 3.13 | Variable not included | Variable used for sensitivity analysis only – see Supplement 2 |

\*Model C includes the following variables: loneliness, social isolation, age, gender and household wealth.

\*\*Model D includes the variables in model C and systolic blood pressure, hypertensive medication use, smoking status, diabetes, HDL and total cholesterol cholesterol.

**Figure 1** Sample selection process

Households dropped, because:

- they did not respond to HSE *n=7,919*;\*

- they did not include an adult aged 50+ or someone living with an adult aged 50+, *n=13,930*;\*

- they did not permit re-interview *n=1,224* (containing 1,951 individuals)

Households selected for participation in the HSE in 1998, 1999 or 2000

 *n=31,051*\*

Households eligible to take part in ELSA

*n=11,578* (containing 18,813 adults aged 50+ or living with someone aged 50+)

People aged 50+ who took part in Wave 1 of ELSA

*n=11,391*

Participants dropped, because:

- they did not complete a questionnaire and take part in the nurse visit, *n=1,751*;

- they reported a heart problem or stroke prior to Wave 2 of ELSA, *n=1,482*;

- they were interviewed by proxy in Waves 3, 4 or 5 of ELSA, *n=150*.

Participants who took part in Wave 2 of ELSA (i.e. the baseline for this study)

*n=8,780*

Participants in our analysis

*n=5397*

\*Note that household numbers only were available for these stages.