The longitudinal relationship between loneliness, social isolation, and frailty in older adults in England: a prospective analysis

Katie Davies, Asri Maharani, Tarani Chandola, Chris Todd, Neil Pendleton

Summary

Background It is estimated that about 10% of people aged 65 and older are frail. Loneliness and social isolation are linked to increased mortality and poorer functional capacity. We assessed trends in frailty status associated with loneliness and social isolation over 14 years in a representative sample of English older adults.

Methods In this longitudinal study, we used data from the English Longitudinal Study of Ageing (ELSA), which was designed to recruit a representative sample of adults aged 50 years and older living in private households in England. We analysed Waves 2–8 (covering June, 2004, to June, 2017). Frailty was defined using the frailty index, analysed continuously and as pre-specified categories, to categorise individuals as being non-frail (≤0·08), pre-frail (>0·08 to <0·25), or frail (≥0·25 to 1·00). Loneliness was measured using the UCLA 3-item Loneliness Scale and social isolation was measured following a previous ELSA approach, and both sets of scores were categorised into low, medium, or high. Linear mixed methods and Cox proportional hazard modelling were used, adjusted for confounders.

Findings The study sample consisted of 9171 participants at the baseline of Wave 2 (4083 male and 5088 female), with similar numbers in subsequent waves. In the fixed effect model, adjusted for marital status, age, gender, wealth, and smoking status, respondents with higher levels of loneliness had a higher frailty index score (β coefficient 0·006, 95% CI 0·006 to 0·007; p<0·0001), as did those with a higher level of social isolation (β 0·002, <0·001 to 0·002; p<0·0001). Increasing age was associated with an increased frailty index, adjusted for loneliness and social isolation independently. Compared with a low level of loneliness, there was a higher risk of developing frailty with medium loneliness (hazard ratio [HR] 1·57, 95% CI 1·49 to 1·65; p<0·0001) and high loneliness (HR 2·62, 2·49 to 2·76; p<0·0001). Compared with a low level of social isolation, there was a higher risk of developing frailty with medium social isolation (HR 1·12, 1·05 to 1·20; p<0·0001) and high social isolation (HR 1·32, 1·22 to 1·43; p<0·0001).

Interpretation Both loneliness and social isolation increase the risk of developing frailty. Understanding these mechanisms might offer opportunities to attenuate this risk.

Funding None.

Lancet Healthy Longev 2021; 2: e70–77

Published Online January 14, 2021 https://doi.org/10.1016/S2666-7568(20)30038-6

See Comment page e54

Manchester University National Health Service Foundation Trust, Manchester, UK (K Davies MBBCh, Prof C Todd PhD); **School of Health Sciences** (A Maharani PhD, Prof C Todd) **and School of Biological Sciences** (Prof N Pendleton FRCP), **Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, and School of Social Sciences, Faculty of Humanities** (Prof T Chandola DPhil), **The University of Manchester, Manchester, UK; National Institute of Health Research Applied Research Collaboration Greater Manchester, Manchester, UK** (Prof C Todd, Prof N Pendleton); **Salford Royal National Health Services Foundation Trust, Manchester, UK** (Prof N Pendleton)

Correspondence to: Katie Davies, Manchester University National Health Service Foundation Trust, Manchester M13 9WL, UK **daviesk@doctors.org.uk**

Introduction

Frailty is an evolving concept that describes an individual's vulnerability to poor resolution of homoeostasis following a sudden change in health status.[1] There are two key clinical models used to assess frailty. Fried's phenotype model[2] defines frailty on the basis of the presence of at least three of five criteria: slow gait speed, low physical activity, self-reported exhaustion, unintentional weight loss, and weak grip strength. Alternatively, Rockwood's cumulative deficit model[3] quantifies frailty using a frailty index, which reflects the accumulation of so-called deficits, whereby a score is computed as the proportion of deficits present divided by the total deficits considered.[3]

With an increasingly ageing population, frailty will place an increasingly substantial burden on health and wellbeing, which in turn will have a considerable effect on social care resources and will carry implications for clinical practice and public health.[4] There is, therefore, a need to identify approaches to attenuate the development of frailty.

Previous research has identified associations between frailty and both modifiable and non-modifiable factors, including age, gender, wealth, clinical factors, such as depression, and lifestyle factors, such as diet.[5] An association that is not fully understood is that between frailty and social functioning, including loneliness and social isolation.[5,6] Social isolation is typically defined as having few or infrequent social contacts. By contrast, loneliness is described as a subjective dissatisfaction with the discrepancy between the actual and preferred level and quality of social contact.[7] These constructs can operate independently: an individual can be socially isolated but not feel lonely, or lonely while having social contacts. This distinction is important when assessing relationships with frailty because they cover different

Research in context

Evidence before this study

Loneliness and social isolation are associated with increased mortality and reduced functional capacity. With an increasingly older population, frailty will increasingly affect health and social care, and an opportunity therefore exists to identify modifiable associations. We searched MEDLINE and OVID, as well as additional reading lists, using the search terms "frail", "frailty", "elderly" and "lonely", "loneliness", and "social isolation", with no language restrictions, from Jan 1, 2000, to Sept 20, 2019. We found that there is a dearth of research investigating the longitudinal relationship between loneliness, social isolation, and frailty.

Added value of this study

To our knowledge, this is the first study to use a 14-year period and large sample size to analyse trajectories of the frailty index and the onset of frailty and their association with social isolation and loneliness. We add to previous longitudinal research, which has shown that only loneliness is associated with frailty.

Implications of all the available evidence

This research suggests that both loneliness and social isolation are associated with increased risk of developing frailty, and therefore provide an opportunity to attenuate that risk. Because loneliness and social isolation are separate constructs and are independently associated with frailty, our findings support interventions that target both and support the need for further research into the effectiveness of such interventions when these constructs are analysed separately.

aspects of social relationships, which can be addressed by different interventions.

There has been growing concern globally about the prevalence of loneliness and social isolation, although figures vary by study population, age, and the measures used to define them.[7] Generally, the older population have smaller social networks and higher loneliness rates, particularly due to declining financial resources, illness, bereavement, and declining mobility. Perissinotto and colleagues[8] found the prevalence of loneliness to be 29% in US participants aged older than 75 years in 2002, and Age UK estimated that a quarter of people aged 50 years or older living in England felt lonely some of the time.[9] With rates of loneliness increasing, a minister was appointed in 2018 as part of the first UK loneliness strategy.[10]

Both loneliness and social isolation have been shown to be associated with increased mortality and reduced functional status.[10–14] Associations have been identified between loneliness and depression, anxiety, stress, sleep, and cognition,[13] and a synergistic relationship between social isolation and loneliness on mortality has been shown, such that higher social isolation is associated with greater effects of loneliness on mortality, and higher loneliness is associated with greater effects of social isolation on mortality.[15]

Frailty has been shown to be associated with loneliness and social isolation in cross-sectional studies.[16,17] Longitudinal data enable patterns to be observed over time, allowing for variation at different timepoints and thus enabling researchers to better capture a consistent state of frailty. However, there is a scarcity of data investigating the longitudinal relationship between loneliness, social isolation, and frailty. Previous research has used the English Longitudinal Study of Ageing (ELSA), which collected rich, multidisciplinary data from a nationally representative sample of older adults. Using ELSA, Gale and colleagues[18] showed that although loneliness predicted higher frailty on the Fried frailty phenotype, it did not predict a higher frailty index, and social isolation did not predict frailty on either measure. However, more recent waves of data collection within the ongoing ELSA programme enable the association between loneliness, social isolation, and frailty to be examined over a longer time period (14 years), and earlier relationships to be re-examined. We aim to add to previous longitudinal modelling research by using multiple timepoints to identify trends over time, reducing between-participant variation and the number of participants needed in order to detect effects. In this study, we aimed to assess the relationship between loneliness, social isolation, and frailty across 14 years in a representative sample of community-dwelling older people in the UK.

Methods

Study design and participants

In this longitudinal study, we used data from ELSA, which was designed to recruit a representative sample of adults aged 50 years and older living in private households in England. Data were collected by the National Centre for Social Research. The first wave of data collection began on March 1, 2002, with subsequent data collection waves every 2 years (Wave 2 to Wave 8) using face-to-face interviews and self-completed questionnaires, and a nurse visit every 4 years for a subset of participants. Wave 8 data were collected until June 30, 2017. Subsequent waves of ELSA data were not included within this study because they were not completed at the time of analysis.[19] To deal with the attrition that often occurs in studies on ageing, there were refreshment samples at Wave 3, Wave 4, Wave 6, and Wave 7. The Wave 1 sample was drawn from Health Survey for England respondents who were 50 years and older; refreshment samples were also

drawn from Health Survey for England respondents but with differing age criteria to correct for the age profile (Wave 3: aged 50–52 years; Wave 4: aged 50–74 years; Wave 6: aged 50–55 years; and Wave 7: aged 50–51 years).[19] The current study used 9171 individuals, aged 50 years and older, from Wave 2 to Wave 8, including refreshment waves, because loneliness and social isolation data were not collected in Wave 1. Ethical approval was obtained from the National Research and Ethics Committee.

Procedures

Data on loneliness and social isolation were collected using self-completed questionnaires in Waves 2–8. The UCLA 3-item Loneliness Scale[20] was used to quantify loneliness. The questions were "How often do you feel you lack companionship?", "How often do you feel left out", and "How often do you feel isolated from others?", for which the response options were (1) "hardly ever or never", (2) "some of the time", or (3) "often". All items were summed arithmetically to provide a loneliness score ranging from 3 to 9, whereby a higher score indicates greater loneliness. Because the data were positively skewed, we categorised scores into low (3), medium (4–5), and high (≥6). For social isolation, we used an approach to ELSA that Gale and colleagues[18] previously used, in which 1 point was allocated for each of the following: not being married or cohabiting; having less than monthly contact with each child, other members of the family, and friends (one point for each); and not being a member of organisations, such as religious groups or social groups. For this scale, scores were summed to provide a social isolation index ranging from 0 to 5, with higher scores indicating higher social isolation. Scores were again positively skewed and were therefore categorised into low (0), medium (1), and high (≥2).

We assessed frailty using the frailty index, whereby we selected information on 59 functional, psychological, and social deficits within the range of data variables in ELSA (appendix p 3).[21,22] We did not include loneliness as a deficit in the frailty score from the list of possible deficits, although it was included in a previously published version.[23] Binary variables were coded as 0 or 1, and for ordinal and continuous variables, coding was based on distribution. Where variables were irreversible (eg, Alzheimer's disease), a score of 1 in one wave was allocated in all subsequent waves. The total number of deficits were summed and divided by total possible deficits, to create a frailty index between 0 and 1, where higher scores indicated greater frailty. Frailty was then categorised using defined cutoff points to indicate an individual being robust (ie, non-frail: ≤0·08), pre-frail (>0·08 to <0·25), or frail (≥0·25 to 1·00).[24]

See Online for appendix

Statistical analysis

We compared baseline characteristics across the categories of loneliness and social isolation (low, medium, and high) using ordinal χ^2 tests for categorical variables and Kruskal-Wallis one-way analysis of variance for numerical variables.

We used linear mixed models to describe the trajectories of frailty and to assess the association of social isolation

	Total (n=9171)	Loneliness score			Social isolation score		
		Low (n=4204)	Medium (n=2202)	High (n=1502)	Low (n=2327)	Medium (n=2112)	High (n=926)
Frailty index	0·2 (0·1)	0·1 (0·1)	0·2 (0·1)	0·2 (0·1)	0·1 (0·1)	0·1 (0·1)	0·2 (0·1)
Age, years	66·3 (10·2)	65·1 (9·3)	65·8 (9·9)	67·2 (10·9)	63·7 (8·3)	66·0 (9·6)	67·6 (10·7)
Gender							
Male	4083 (44·5%)	2017 (48·0%)	972 (44·1%)	537 (35·8%)	1085 (46·6%)	831 (39·3%)	422 (45·6%)
Female	5088 (55·5%)	2187 (52·0%)	1230 (55·9%)	965 (64·2%)	1242 (53·4%)	1281 (60·7%)	504 (54·4%)
Ethnicity							
White, n (%)	8952 (97·6%)	4163 (99·0%)	2158 (98·0%)	1465 (97·5%)	2296 (98·7%)	2082 (98·6%)	913 (98·6%)
Other, n (%)	219 (2·4%)	41 (1·0%)	44 (2·0%)	37 (2·5%)	31 (1·3%)	30 (1·4%)	13 (1·4%)
Marital status							
Single	470 (5·1%)	154 (3·7%)	113 (5·1%)	104 (6·9%)	2 (0·1%)	9 (0·4%)	5 (0·5%)
Married	6060 (66·1%)	3355 (79·8%)	1434 (65·1%)	673 (44·8%)	2238 (96·2%)	1330 (63·0%)	382 (41·3%)
Divorced	975 (10·6%)	289 (6·9%)	247 (11·2%)	253 (16·8%)	64 (2·8%)	283 (13·4%)	211 (22·8%)
Widowed	1665 (18·2%)	406 (9·7%)	408 (18·5%)	471 (31·4%)	23 (1·0%)	490 (23·2%)	328 (35·4%)
Smoker status							
Non-smoker	3054 (33·3%)	1415 (33·7%)	721 (32·7%)	496 (33·0%)	836 (35·9%)	724 (34·3%)	247 (26·7%)
Ex-smoker	4699 (51·2%)	2236 (53·2%)	1131 (51·4%)	723 (48·1%)	1246 (53·5%)	1079 (51·1%)	474 (51·2%)
Current smoker	1418 (15·5%)	553 (13·2%)	350 (15·9%)	283 (18·8%)	245 (10·5%)	309 (14·6%)	205 (22·1%)
Wealth	3·0 (0·01)	3·3 (1·4)	3·0 (1·4)	2·7 (1·4)	3·5 (1·4)	3·0 (1·4)	2·7 (1·4)

Data are mean (SD) or n (%). Loneliness and social isolation data were not available for all participants. A score for individual wealth was derived from net financial wealth. This was gross financial wealth with financial debts subtracted.

Table 1: **Baseline characteristics**

	Hazard ratio* (95% CI)	p value
Loneliness score		
Low	1·00	Reference
Medium	1·57 (1·49–1·65)	<0·0001
High	2·62 (2·49–2·76)	<0·0001
Social isolation score		
Low	1·00	Reference
Medium	1·12 (1·05–1·20)	<0·0001
High	1·32 (1·22–1·43)	<0·0001

*Adjusted for gender, age, marital status, smoking status, and wealth.

Table 2: **Association between frailty incidence and social isolation and loneliness group adjusted for confounders using the proportional hazards model**

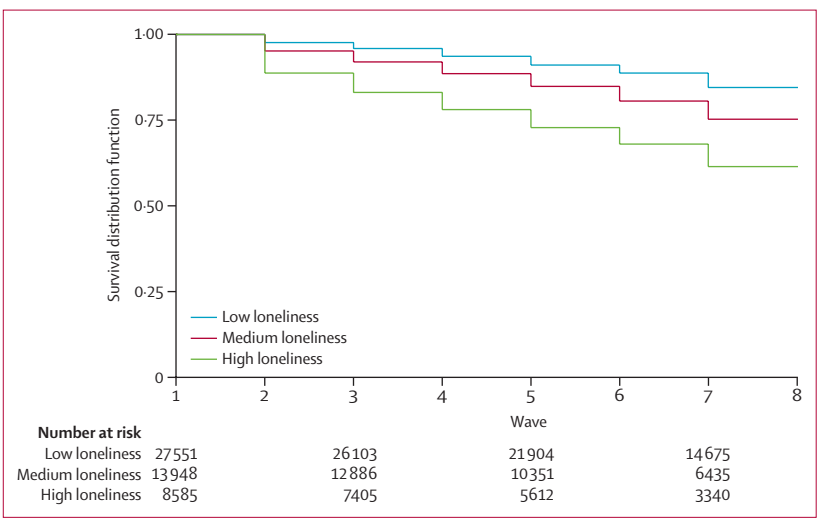

Figure 1: **Kaplan-Meier analysis of unadjusted frailty trajectories according to loneliness level using the proportional hazards model**

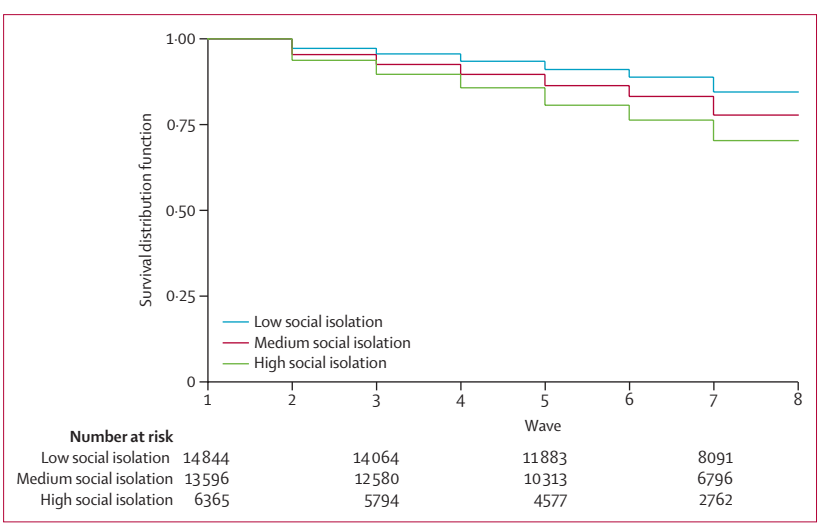

Figure 2: **Kaplan-Meier analysis of unadjusted frailty trajectories according to social isolation level using the proportional hazards model**

and loneliness with the frailty index, considered as a continuous measure. The model used social isolation and loneliness at Wave 2 as the baseline, and then observed the frailty index in each subsequent wave up to Wave 8, as the respondents became about 14 years older. We first analysed the linear mixed model estimates for the frailty index with social isolation and loneliness separately. For each analysis we adjusted for covariates identified within the literature: marital status, age, smoking status, education status, ethnicity, wealth, and gender. A score for individual wealth was derived from net financial wealth. This was gross financial wealth with financial debts subtracted. For ethnicity, we included White and Black, Asian, and Minority Ethnic groups. We used a quadratic model on the basis of a prediction that the trajectories might take a curvilinear form. In a further analysis, both social isolation and loneliness were entered into the same adjusted model to examine differential effects on the frailty index. We analysed both the fixed and random effects models to assess the panel structure of the data, and we used the Hausman test to distinguish between the models. In addition, we tested the association of loneliness and social isolation as categorical measures with the observed frailty trajectories.

The multivariate association between social isolation and loneliness was analysed for frailty categories of robust, pre-frail, and frail, using the Cox proportional hazard model, with study wave as the timescale that was adjusted for covariates. This approach enabled us to estimate the relative risk of frailty with differing levels of loneliness and social isolation. Respondents classified as frail at baseline were excluded from the analysis. Our first analysis modelled the risk of developing frailty depending on the level of loneliness while censoring for study drop out or Wave 8, whichever occurred first. We then repeated the analysis for the risk of developing frailty depending on the level of social isolation. There were some missing data within the social function variables, which we tried to correct for using multiple imputation. Data were analysed using Stata (version 15).

Role of the funding source

This work was not funded. All authors had full access to all the data, and the corresponding author had the final responsibility to submit for publication.

Results

The study sample consisted of 9171 participants at the Wave 2 baseline (4083 male and 5088 female). There were similar numbers of participants in subsequent waves (Wave 3: 9344; Wave 4: 10749; Wave 5: 10094; Wave 6: 10372; Wave 7: 9491; and Wave 8: 8355). At baseline, the mean age of participants was 66·3 years (SD 10·2) and there were 8952 (97·6%) White participants (table 1). 6060 (66·1%) of 9171 participants were married, 1418 (15·5%) were current smokers, and the mean frailty index was 0·2 (SD 0·1; table 1). Among the baseline

participants, 2843 (31·0%) were classed as robust, 4641 (50·6%) as pre-frail, and 1697 (18·5%) as frail. 4204 (53·2%) of 7908 participants with available data on loneliness were categorised as having a low level of loneliness, compared with 2202 (27·8%) with a medium level and 1502 (19·0%) with a high level. 2327 (43·4%) of 5365 participants with available data on social isolation reported a low level of social isolation, compared with 2112 (39·4%) with a medium level and 926 (17·3%) with a high level. The bivariate analyses showed that both high and medium loneliness and high and medium social isolation were independently associated with a higher frailty index (table 1). Respondents with high and medium loneliness and social isolation were more likely to be single, divorced, or widowed, as well as current smokers and less wealthy (table 1). In addition, high levels of loneliness were reported by respondents who were female and from minority ethnic groups (table 1).

Table 2 shows the estimated hazard ratios (HRs) for developing frailty across the study waves according to level of loneliness and social isolation. In the final models for both loneliness and social isolation, gender, age, marital status, ethnicity, education status, smoking status, and wealth were adjusted for, with no terms considered as random. Study wave was used as the timescale for the risk of frailty development. Different start times for the refreshment sample waves were accounted for within the analysis. Compared with a low level of loneliness, there was a significantly higher relative risk of developing frailty with medium loneliness (HR 1·570; 95% CI 1·49 to 2, 1·65; p<0·00012) and a higher relative risk with high loneliness (HR 2·62, 2·49 to 2·76; p<0·0001). Similarly, compared with a low level of social isolation, there was a significantly higher relative risk of developing frailty with medium social isolation (HR 1·12, 1·05 to 1·20; p<0·0001) and high social isolation (HR 1·32, 1·22 to 1·43; p<0·0001).

As shown in the Kaplan-Meier analyses for unadjusted rates of frailty for each level of loneliness (figure 1) and level of social isolation (figure 2), there was an increased risk of developing frailty with increasing loneliness and social isolation.

In the random effects model, we included marital status, age, smoking status, education status, ethnicity, gender, frailty and loneliness, social isolation, or both (table 3). Respondents who reported a higher level of loneliness had a significantly higher frailty index (β coefficient 0·010, 95% CI 0·009 to 0·010; p<0·0001; table 3). The association remained significant when social isolation was included within the analysis (β 0·010, 0·009 to 0·010; p<0·0001). A higher level of social isolation was associated with a higher frailty index score in the independent model (β 0·001, 0·003 to 0·005; p<0·0001), and it remained significant in the joint model (β 0·003, 0·002 to 0·004; p<0·0001).

The predicted trajectory of the frailty index scores by age for the three levels of loneliness and for the three levels

	β coefficient for association between frailty and loneliness (n=54 126 observations)				β coefficient for association between frailty and social isolation (n=37 255 observations)				β coefficient for association between frailty and social isolation and loneliness (joint model; n=36 719 observations)			
	Random effects model	p value	Fixed effects model	p value	Random effects model	p value	Fixed effects model	p value	Random effects model	p value	Fixed effects model	p value
Gender (female)	0·015 (0·012 to 0·018)	<0·0001	Omitted	NA	0·018 (0·014 to 0·022)	<0·0001	Omitted	NA	0·017 (0·013 to 0·020)	<0·0001	Omitted	NA
Ethnicity (Caucasian)	–0·026 (–0·035 to –0·017)	<0·0001	Omitted	NA	–0·029 (–0·040 to –0·019)	<0·0001	Omitted	NA	–0·023 (–0·034 to –0·014)	<0·0001	Omitted	NA
Marital status (single)	0·002 (0·001 to 0·003)	0·0050	0·002 (<0·001 to 0·003)	0·034	0·006 (0·004 to 0·007)	<0·0001	0·005 (0·003 to 0·006)	<0·0001	0·002 (<0·001 to 0·003)	0·023	0·002 (0·001 to 0·004)	0·010
Age	–0·007 (–0·008 to –0·006)	<0·0001	–0·012 (–0·013 to –0·011)	<0·0001	–0·008 (–0·009 to –0·007)	<0·0001	–0·012 (–0·013 to –0·011)	<0·0001	–0·007 (–0·008 to –0·006)	<0·0001	–0·012 (–0·013 to –0·010)	<0·0001
Smoker status (non-smoker)	0·004 (0·002 to 0·005)	<0·0001	–0·008 (–0·010 to –0·006)	<0·0001	0·005 (0·003 to 0·007)	<0·0001	–0·007 (–0·010 to <–0·005)	<0·0001	0·005 (0·003 to 0·007)	<0·0001	–0·007 (–0·010 to –0·005)	<0·0001
Wealth (higher)	–0·005 (–0·006 to –0·005)	<0·0001	–0·001 (–0·002 to –<0·001)	0·0010	–0·005 (–0·006 to –0·004)	<0·0001	–0·001 (–0·002 to <–0·001)	0·019	–0·005 (–0·006 to –0·004)	<0·0001	–0·001 (–0·001 to <–0·001)	0·037
Education level (higher)	–0·010 (–0·011 to –0·009)	<0·0001	Omitted	NA	–0·010 (–0·011 to –0·008)	<0·0001	Omitted	NA	–0·010 (–0·010 to –0·008)	<0·0001	Omitted	NA
Loneliness level (high)	0·010 (0·009 to 0·010)	<0·0001	0·006 (0·006 to 0·007)	<0·0001	NA	NA	NA	NA	0·010 (0·009 to 0·010)	<0·0001	0·006 (0·005 to 0·007)	<0·0001
Social isolation level (high)	NA	NA	NA	NA	0·001 (0·003 to 0·005)	<0·0001	0·002 (<0·001 to 0·002)	0·0010	0·003 (0·002 to 0·004)	<0·0001	0·001 (–0·001 to 0·002)	0·075
Intercept	0·264 (0·232 to 0·297)	<0·0001	0·388 (0·355 to 0·422)	<0·0001	0·417 (0·282 to 0·361)	<0·0001	–0·435 (0·375 to 0·459)	<0·0001	0·256 (0·217 to 0·296)	<0·0001	0·387 (0·344 to 0·429)	<0·0001

Data are n (95% CI). The random effects model was adjusted for gender, age, marital status, smoking status, and wealth, including the quadratic term for age. The fixed effects model was adjusted for marital status, age, and smoking status, including the quadratic term for age. Education status, ethnicity, and gender were omitted from the model. ELSA=English Longitudinal Study of Ageing. NA=not applicable.

***Table 3*: Longitudinal associations between loneliness and social isolation and frailty: β coefficients predicting the frailty index in Waves 2–8 in ELSA**

	β coefficient (95% CI)	p value
Loneliness (n=54 124 observations)		
Low	Reference	..
Medium	0·012 (0·011 to 0·013)	<0·0001
High	0·035 (0·032 to 0·036)	<0·0001
Social isolation (n=37 254 observations)		
Low	Reference	..
Medium	0·004 (0·002 to 0·005)	<0·0001
High	0·012 (0·009 to 0·013)	<0·0001

Coefficients adjusted for gender, age, marital status, smoking status, and wealth.

Table 4: **Longitudinal association between loneliness and social isolation group and frailty using the growth model**

of social isolation are presented in the appendix (pp 1–2). After controlling for marital status, age, smoking status, education status, ethnicity and gender, the trajectories of frailty index took linear shapes and remained significant following the addition of a quadratic term for age (which was used to confirm the model had not forced a linear distribution). The trajectories show that increasing age is associated with an increasing frailty index predicted by a higher level of loneliness (appendix p 1). Similarly, increasing age increased the frailty index predicted by the loneliness group, and also increased the frailty index predicted by the social isolation group (appendix p 2). According to the Hausman statistical test, the random effects model was rejected in favour of the fixed effects model (p<0·0001), shown in table 3. The final model included marital status, age, smoking status, wealth, and frailty, as well as loneliness, social isolation, or both. Education status, ethnicity, and gender were omitted from the model, which already adjusts for these constant variables.

In the fixed effects model, respondents who reported higher levels of loneliness had a significantly higher frailty index score (β 0·006, 95% CI 0·006 to 0·007; p<0·0001; table 3). The association remained significant when social isolation was included (β 0·006, 0·005 to 0·007; p=0·0010). A higher level of social isolation was associated with a significantly higher frailty index score in the independent model (β 0·002, <0·001 to 0·002; p<0·0001), which remained significant in the joint model (β 0·001, <–0·001 to 0·002; p<0·0001).

Table 4 shows the linear mixed methods models for categories of loneliness and social isolation. There was a significant association (p<0·0001) between increasing loneliness and social isolation and increased frailty index.

As marital status formed part of the social isolation variable, adjusting for it might have affected the results. Therefore, a repeat analysis was done in which marital status was removed from the model. Results showed that in the joint model, respondents had higher frailty scores when they had a higher level of loneliness (β 0·006, 95% CI 0·006 to 0·007; p<0·0001) and social isolation (β 0·001, 0·001 to 0·002; p<0·0001).

Discussion

To our knowledge, this is the first study to use a broad period of 14 years and a large sample size to analyse the association between social isolation, loneliness, and trajectories of the frailty index and the onset of frailty. Loneliness and social isolation were independently associated with increased frailty across the study waves. The associations remained significant when both loneliness and social isolation were included in a joint model. Compared with a low level of loneliness, there was a higher risk of developing frailty with medium loneliness (HR 1·57) and high loneliness (HR 2·62). In addition, compared with low social isolation, there was a higher risk of frailty with medium social isolation (HR 1·12) and high social isolation (HR 1·32).

Prospective longitudinal research assessing the effects of loneliness and social isolation on frailty has been scarce. Hoogendijk and colleagues[17] used the Longitudinal Aging Study Amsterdam across 3 years to show that reduced social functioning (including loneliness) was associated with greater levels of frailty phenotype in the Netherlands. Gale and colleagues[18] used both the frailty index and phenotype models of frailty across Waves 2–5 of ELSA and found only an association between the frailty phenotype and loneliness, defined using the UCLA 3-item score, but not the frailty index. In contrast, our results, using Waves 2–8 of ELSA, show an association between increased loneliness and increased risk of frailty using the frailty index. Despite using the same dataset and loneliness scoring system, Gale and colleagues[18] had a much smaller sample size due to the use of fewer waves and the inclusion of only those participants with complete data to form both the frailty scoring systems, which could explain the difference in findings.

Strawbridge and colleagues[25] found that, although their unadjusted results suggested a relationship between frailty (based on 16 variables) and social isolation (defined by meeting two of three criteria in having fewer than three friends or relatives and seeing fewer than three of either in the past month), this relationship was not statistically significant. Gale and colleagues[18] also found no longitudinal association between social isolation (defined using the same score as in the current study) and both the frailty phenotype and frailty index. These studies focused on older adults. Our results, using more waves within ELSA, show that a higher level of social isolation is related to increased frailty index and increased risk of developing frailty.

Our study results suggest that both the quantity and perceived quality of social interactions and relationships can adversely affect functioning. A person's subjective negative feeling about their level of contact increases their risk of frailty. Loneliness has been shown to affect neuroendocrine function, with studies showing worse cardiovascular health and biological function in frail individuals.[7,16] Lonely individuals are also thought to have worse health behaviours (ie, poorer lifestyles and nutrition,

more smoking and alcohol use, and less exercise) than individuals who are not lonely.[7] Loneliness has also been associated with worse sleep patterns and reduced quantity of sleep. Another hypothesised mechanism for the association between loneliness and frailty is poorer gait speed and mobility,[12] both of which are associated with loneliness and predispose individuals to sarcopenia, an age-related reduction in muscle mass, which is a risk factor for frailty.[11] However, since gait speed and mobility are also markers of frailty, the usefulness of this insight is limited. In addition, loneliness can increase negative thoughts and reduce resilience, and rates of stress and depression are higher in lonely individuals than in individuals who are not lonely, thereby increasing the development and progression of physical illness and disease.[7]

We also showed that a reduced quantity of social contact increases frailty regardless of whether the individual perceives this to be negative. Similar to loneliness, worse health behaviours and increased cardiovascular disease and mental health difficulties have been shown in socially isolated individuals.[14,26] Choi and colleagues show that social isolation increases sleep disturbance, depression, and fatigue in older adults, but that subjective social isolation contributes more significantly than objective measures.[27] It could also be hypothesised that individuals who experience greater social isolation might have reduced access to immediate support for health needs due to infrequent contact with others, which could lead to increased frailty. Social isolation is a risk factor for loneliness, and this association could increase the risk of frailty.[15] There is currently no evidence showing whether loneliness is also a risk factor for social isolation. Further research is needed to understand these links.

Different measures of loneliness, social isolation, and frailty could create differences in observed associations. Multiple-item scoring systems for loneliness include the 3-item and 20-item UCLA Loneliness Scale and the DeJong Gierveld Loneliness Scale, and measures for social isolation include the Berkman-Syme Social Network Index and the Lubben Social Network Scale. Multiple-item scores enable a greater window for observation but their use in retrospective analyses is limited because specific data must be collected to form a score and there are time constraints when designing prospective studies with larger scales (eg, 20-item scales). We used the 3-item UCLA Loneliness Scale and a 5-item social isolation scoring system that was applicable to ELSA data, and therefore differences between our findings and those of other studies might be explained by the use of different scoring systems.

Similarly, frailty scoring systems capture different constructs, with the frailty phenotype using physical dimensions of frailty and the frailty index using psychological and social dimensions in addition to physical ones.[28] This broader approach of the frailty index can affect the prevalence and incidence of frailty estimates, as it typically quantifies more participants as frail and therefore allows a greater assessment of frailty in different waves. Research findings should be interpreted with consideration of the measures used.

Different types of interventions have been trialled to improve social functioning using varying group sizes and intervention goals.[29–31] Interventions aiming to increase social interaction might not improve loneliness and vice versa.[31] Interventions targeting loneliness generally work to help individuals make interpersonal ties (eg, befriending activities) and improve social bonding and coping strategies, while those targeting social isolation aim to increase social contact (eg, technology-based services, community activities, and home visits).[31] Because social isolation is a risk factor for loneliness, some activities can be targeted at both. The wide range in interventions and individual responses makes assessment of effectiveness difficult, so an individualised approach could be needed.[31]

At the time of publication, older adults are being advised to shield to minimise their risk of contracting COVID-19. There is concern that those previously not reported to be lonely or socially isolated are at a disproportionately increased risk of becoming so during the pandemic. This risk could be due to reduced attendance at community events, difficulties for older adults in using digital technology for communication, and reduced daily contact. Although our results may not be generalisable, we did identify mechanisms to attenuate frailty by reducing loneliness and social isolation, which is particularly important at a time of reduced social contact.

The main strength of the current study is the use of a large dataset, assessments across multiple waves, and a dataset that is nationally representative of people aged 50 years and older, using Health Survey for England data. The study limitations include the low level of representativeness of ethnicity in ELSA. There were also missing data for the social isolation scale, which could have affected the results. A limitation of using a fixed effects model is that results are less generalisable. Previous research shows a bi-directional relationship between frailty and social functioning, with social functioning associated with the development of frailty and frailty adversely affecting social functioning, possibly due to declining mobility, and, as such, our research cannot prove causality.[17,18] Future research using randomised controlled trials or complex statistical methods is required to establish a causal relationship and to assess the interaction between loneliness and social isolation.

In conclusion, both loneliness and social isolation are associated with frailty longitudinally and are predictors of frailty risk. Loneliness and social isolation are highly prevalent in older people and are linked to higher mortality and poorer functional status. Our study of loneliness and social isolation across a large timespan has provided a greater understanding of their association with frailty, which could inform the design and implementation of interventions.

Contributors
AM, CT, and NP were responsible for the study design. KD and AM did the data collection, data analysis, and data interpretation. KD drafted the manuscript. KD, AM, TC, CT, and NP revised the manuscript and approved the final version.

Declaration of interests
We declare no competing interests.

Data sharing
ELSA data were available through the UK Data Archive and are widely available to access in this way; as such, our study data will not be made available for access.

Acknowledgments
CT and NP are affiliated to a unit funded by the UK National Institute for Health Research.

References

1 Rockwood K, Howlett SE. Fifteen years of progress in understanding frailty and health in aging. *BMC Medicine* 2018; **16:** 220.
2 Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; **56:** m146–56.
3 Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005; **173:** 489–95.
4 Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet* 2013; **381:** 752–62.
5 Fried L, Prohaska T, Burholt V, et al. A unified approach to loneliness. *Lancet* 2020; **395:** 114.
6 Nicholson NR. A review of social isolation: an important but underassessed condition in older adults. *J Prim Prev* 2012; **33:** 137–52.
7 Ong AD, Uchino BN, Wethington E. Loneliness and health in older adults: a mini-review and synthesis. *Gerontology* 2016; **62:** 443–49.
8 Perissinotto CM, Stijacic Cenzer I, Covinsky KE. Loneliness in older persons: a predictor of functional decline and death. *Arch Intern Med* 2012; **172:** 1078–83.
9 Age UK. All the lonely people: loneliness in later life. September, 2018. https://www.ageuk.org.uk/globalassets/age-uk/documents/reports-and-publications/reports-and-briefings/loneliness/loneliness-report_final_2409.pdf (accessed Jan 5, 2021).
10 Department for Digital, Culture, Media and Sport, UK Government. A connected strategy: a strategy for tackling loneliness—laying the foundations for change. October, 2018. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/750909/6.4882_DCMS_Loneliness_Strategy_web_Update.pdf (accessed Aug 31, 2020).
11 Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspect Psychol Sci* 2015; **10:** 227–37.
12 Shankar A, McMunn A, Demakakos P, Hamer M, Steptoe A. Social isolation and loneliness: prospective associations with functional status in older adults. *Health Psychol* 2017; **36:** 179–87.
13 Cacioppo JT, Hawkley LC, Thisted RA. Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. *Psychol Aging* 2010; **25:** 453–63.
14 Leigh-Hunt N, Bagguley D, Bash K, et al. An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health* 2017; **152:** 157–71.
15 Beller J, Wagner A. Loneliness, social isolation, their synergistic interaction, and mortality. *Health Psychol* 2008; **37:** 808–13.
16 Herrera-Badilla A, Navarrete-Reyes AP, Amieva H, Avila-Funes JA. Loneliness is associated with frailty in community-dwelling elderly adults. *J Am Geriatr Soc* 2015; **63:** 607–09.
17 Hoogendijk EO, Suanet B, Dent E, Deeg DJ, Aartsen MJ. Adverse effects of frailty on social functioning in older adults: results from the Longitudinal Aging Study Amsterdam. *Maturitas* 2016; **83:** 45–50.
18 Gale CR, Westbury L, Cooper C. Social isolation and loneliness as risk factors for the progression of frailty: the English Longitudinal Study of Ageing. *Age Ageing* 2018; **47:** 392–97.
19 Steptoe A, Breeze E, Banks J, Nazroo J. Cohort profile: English Longitudinal Study of Ageing. *Int J Epidemiol* 2013; **42:** 1640–48.
20 Hughes ME, Waite LJ, Hawkley LC, Cacioppo JT. A short scale for measuring loneliness in large surveys: results from two population-based studies. *Res Aging* 2004; **26:** 655–72.
21 Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. *BMC Geriatr* 2008; **8:** 24.
22 Wade KF, Marshall A, Vanhoutte B, Wu FCW, O'Neill TW, Lee DM. Does pain predict frailty in older men and women? Findings from the English Longitudinal Study of Ageing (ELSA). *J Geront A Biol Sci Med Sci* 2016; **72:** 403–09.
23 Watts PN, Blane D, Netuveli G. Minimum income for healthy living and frailty in adults over 65 years old in the English Longitudinal Study of Ageing: a population-based cohort study. *BMJ Open* 2019; **9:** e025334.
24 Romero-Ortuno R. An alternative method for frailty index cut-off points to define frailty categories. *Eur Geriatr Med* 2013; **4:** 299–303.
25 Strawbridge WJ, Shema SJ, Balfour JL, Higby HR, Kaplan GA. Antecedents of frailty over three decades in an older cohort. *J Gerontol B Psychol Sci Soc Sci* 1998; **53:** S9–16.
26 Kobayashi LC, Steptoe A. Social isolation, loneliness, and health behaviors at older ages: longitudinal cohort study. *Ann Behav Med* 2018; **52:** 582–93.
27 Choi H, Irwin MR, Cho HJ. Impact of social isolation on behavioral health in elderly: systematic review. *World J Psychiatry* 2015; **5:** 432.
28 Cesari M, Gambassi G, van Kan GA, Vellas B. The frailty phenotype and the frailty index: different instruments for different purposes. *Age Ageing* 2013; **43:** 10–12.
29 Victor C. An overview of reviews: the effectiveness of interventions to address loneliness at all stages of the life-course. October, 2018. https://whatworkswellbeing.org/wp-content/uploads/2020/01/Full-report-Tackling-loneliness-Oct-2018_0151580300.pdf (accessed Nov 10, 2020).
30 Masi CM, Chen H, Hawkley LC, Cacioppo JT. A meta-analysis of interventions to reduce loneliness. *Pers Soc Psychol Rev* 2010; **15:** 219–66.
31 Fakoya, OA, McCorry NK, Donnelly M. Loneliness and social isolation interventions for older adults: a scoping review of reviews. *BMC Public Health* 2020; **20:** 129.