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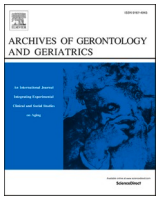

The association of loneliness and social isolation with multimorbidity over 14 years in older adults in England: A population-based cohort study

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HIGHLIGHTS

- The relationship between multimorbidity loneliness and social isolation is unclear.
- We assess bidirectional associations between these constructs over time.
- We find a bidirectional association between loneliness and multimorbidity.
- No significant prospective associations between multimorbidity and social isolation.
- Interventions targeting loneliness may prevent and improve multimorbidity outcomes.

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ABSTRACT

Background: Previous longitudinal studies have linked multimorbidity to loneliness (feeling alienated) and social isolation (having reduced social contact). However, the nature of these associations over time is unclear.
Objective: To examine bidirectional associations of multimorbidity with loneliness and social isolation over a 14-year follow-up in a nationally representative cohort of adults aged ≥ 50 years.
Methods: This retrospective cohort study used seven waves of data (collected between 2004/2005 and 2018/2019) from adults in the English Longitudinal Study of Ageing. Multimorbidity was defined as the presence of ≥2 long-term conditions. Loneliness was measured using the 3-item University of California Los Angeles (UCLA) scale. Social isolation was derived based on cohabitation status, frequency of contact with children, relatives, and friends, and social organisation membership. We used Cox proportional hazards models adjusted for social isolation or loneliness, demographic and health behaviour variables.
Results: The cohort consisted of 6031 adults with baseline and follow-up data on loneliness, social isolation, multimorbidity, and other covariates. Loneliness was associated with increased risk of incident multimorbidity [aHR (95 % CI): 1.38 (1.15–1.65)], whereas social isolation was not [aHR (95 % CI): 0.97 (0.81–1.16)]. Multimorbidity was associated with increased risk of incident loneliness [aHR (95 % CI): 1.55 (1.30–1.84)], but not significantly associated with subsequent risk of incident social isolation [aHR (95 % CI): 1.09 (0.92–1.28)].
Conclusions: An independent bidirectional association exists between loneliness and multimorbidity. Interventions targeting loneliness may prevent or delay multimorbidity and also improve wellbeing for people with multimorbidity.

1. Introduction

Multimorbidity, also known as multiple long-term conditions, is defined as the presence of two or more long-term conditions in an individual (World Health Organization, 2016). More than a third of adults living in England have multimorbidity, with higher prevalence in older adults (Cassell et al., 2018; Head et al., 2021). Multimorbidity is associated with functional limitations, poorer quality of life, increased

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risk of mortality and higher use and cost of health and social care services (Nunes et al., 2016; Soley-Bori et al., 2020). As prevalence of multimorbidity is expected to increase further by 2035 (Kingston et al., 2018), there is a growing need to identify modifiable risk factors for multimorbidity.

Around a third of UK older adults experience loneliness (Victor & Yang, 2012), likely due to changes in life circumstances such as retirement, bereavement, loss of social roles and shrinking social networks. Loneliness (a distressing feeling of alienation due to a discrepancy between one's perceived and desired social relationships) and social isolation (an objective measure of reduced social network size and lack of social contact) have been linked to increased risk of single conditions such as depression, anxiety, dementia, cardiovascular disease, premature mortality, and more recently, multimorbidity (Sundström et al., 2020; Cantarero-Prieto et al., 2018; Hodgson et al., 2020; Singer et al., 2019; Hajek et al., 2020; Hounkpatin et al., 2024). Most studies on the association of multimorbidity with loneliness or social isolation have used cross-sectional designs and reported a significant positive association (Hajek et al., 2020; Hounkpatin et al., 2024).

Longitudinal studies on the association between multimorbidity and social isolation are scarce and only few longitudinal studies on the association of multimorbidity with loneliness exist (Hajek et al., 2020; Hounkpatin et al., 2024). These studies have produced mixed findings on whether changes in multimorbidity relate to changes in loneliness over time (Cantarero-Prieto et al., 2018; Schübbe et al., 2023; Hajek & König, 2020). There is also a lack of studies that assess associations between multimorbidity and loneliness or social isolation over longer follow-up periods. Existing studies on this topic have examined associations over short follow-up periods of two years (Pengpid & Peltzer, 2023; Sieber et al., 2023). These studies may be susceptible to reverse causality. For example, an observed association between loneliness and subsequent multimorbidity two years later could be due to an underlying disease state that influenced loneliness, rather than loneliness itself. Furthermore, the direction of the association of multimorbidity with loneliness and social isolation is unclear. Existing studies have reported either on the association between loneliness and subsequent multimorbidity or the association between multimorbidity and subsequent loneliness. Although it is likely a bidirectional association exists, no study has examined both directions of the relationship in the same cohort. Evidence for a bidirectional relationship can help inform the development of more effective interventions aimed at improving healthy ageing in individuals. Existing studies in the literature have also not examined the association of multimorbidity with both loneliness and social isolation. As loneliness and social isolation are related, it is possible that they may influence the association of the other with multimorbidity. Understanding whether they have independent associations with multimorbidity would further inform whether interventions need to target both loneliness and social isolation, and shed light on mechanisms linking social connection with multimorbidity.

This study aimed to assess bidirectional associations of multimorbidity with loneliness and social isolation over a 14-year follow-up period in a population-based cohort.

2. Methods

2.1. Study design and participants

The English Longitudinal Study of Ageing (ELSA) is an ongoing representative cohort study of adults aged ≥50 years living in private households in England. The ELSA sample is based on households that participated in the Health Survey for England (HSE) in 1998,1999, or 2001. ELSA collects detailed information on sociodemographic, clinical, biological, psychological, lifestyle, economic and social variables. The first wave of data collection was in 2002–2003 and participants were interviewed biennially (using face-to-face interviews and self-completion questionnaires), with an additional nurse visit every four years. Refreshment samples (also drawn from HSE, with differing age criteria) were added at Waves 3,4,6,7, and 9 to allow ELSA to remain representative of individuals aged ≥50 years. Full details of the methodology, including sampling design, non-response and weighting can be found elsewhere (Steptoe et al., 2013; Banks et al., 2018).

This study used data from 2004/2005–2018/2019 (Waves 2–9) as data on loneliness and social isolation were not collected during 2002–2003 (Wave 1). For this study, we included partners of initial participants and refreshments from later waves. We defined baseline as the first wave of data collection at which a participant was aged ≥50 years.

Ethical approval for the survey was obtained from the National Health Service (NHS) Research Ethics Committees under the National Research and Ethics Service (NRES). This study was approved by the University of Southampton Faculty of Medicine Research Committee (67,953).

2.2. Procedures

Loneliness and social isolation were assessed at Waves 2 to 9 of the ELSA survey. Loneliness was assessed using the three-item University of California Los Angeles (UCLA) Loneliness scale (Hughes et al., 2004). Participants were asked the frequency of feeling: (1) a lack of companionship (2) left out or (3) isolated from others. Possible responses were: hardly ever or never (score: 1), some of the time (score: 2), often (score: 3). Scores were summed and ranged from 3 to 9, with higher scores indicating higher levels of loneliness. Scores were positively skewed and therefore grouped as not lonely (a score of 3) or medium or lonely (≥4). Social isolation was assessed as a score of 0 to 5 based on the following five items (one point for each): not being married or cohabitating; having 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 being a member in any civic organisations (e.g.: political parties, neighbourhood groups, religious groups, charitable organisations, religious groups), leisure groups (e.g.: sports clubs, evening classes), or committees (Shankar et al., 2011). Higher scores indicated greater social isolation. Scores were positively skewed and grouped as not socially isolated (a score of 0) or socially isolated (≥1). At each wave, participants were asked whether a doctor had ever told (diagnosed) them that they had any of 15 long-term conditions. Multimorbidity was defined as ever having been diagnosed with ≥2 of the following conditions: hypertension, diabetes, cancer, angina, myocardial infarction, congestive heart failure, heart murmur, arrhythmia, stroke, chronic lung disease (including chronic bronchitis, emphysema, and asthma), mental health disorders (comprising affective conditions [depression, anxiety, emotional problems] and psychotic conditions [hallucinations, schizophrenia, psychosis]), arthritis, Parkinson's disease and dementia (including memory impairment or Alzheimer's disease). These conditions were selected based on consensus work on condition inclusion in defining multimorbidity (Ho et al., 2022; Dambha-Miller et al., 2023).

Data on demographic and behavioural variables were collected at each wave and were included as covariates. Covariates selected were: age [continuous], sex [male or female], ethnicity [white, non-white], marital status [married/cohabitating or never married/divorced/separated/widowed], total household wealth, level of education [no qualification, intermediate (NVQ1/CSE or NVQ2/GCE O level or NVQ3/GCE A level or higher education below degree), and degree level (NVQ4/NVQ5/degree or equivalent)], socioeconomic status (managerial and professional, intermediate, routine and manual), total household wealth, smoking status [non-smoker, smoker], physical activity level [sedentary/low, moderate, high], alcohol consumption [not at all in last 12 months, 1–2 times a year or every couple of months, once or twice a month, once or twice a week, 3–6 days a week, almost daily]. Covariate data at each wave were used in the analyses.

2.3. Statistical analysis

Descriptive statistics were used to summarise patient characteristics, both overall and by loneliness, social isolation and multimorbidity status. The longitudinal association between loneliness and incident (newly-occurring) multimorbidity over the follow-up period was assessed using mixed-effects Cox proportional hazards models for panel data to account for clustering of observations within the individual. The baseline hazard was modelled using the exponential distribution. Study wave was used as the proxy of event time since exact date of diagnoses was not available. Participants with multimorbidity at baseline were excluded from the analyses of incident multimorbidity. We adjusted for confounders (some of which may be conceptualised as possible mediators) based on the literature. Individuals were censored the first time they met the criteria for multimorbidity, or at the end of follow-up for those who did not develop multimorbidity. Model 1 assessed risk of incident multimorbidity from loneliness status at baseline. Model 2 assessed risk of incident multimorbidity from loneliness and social isolation. Model 3 additionally adjusted for age, sex, ethnicity, marital status, socioeconomic status and education status. Model 4 additionally adjusted for smoking status, alcohol consumption and physical activity. Similar models were fitted to examine the association between social isolation and incident multimorbidity (after excluding participants with multimorbidity at baseline). The reverse relationship - the association of multimorbidity at baseline with incident loneliness and incident social isolation (separately) was also assessed using a series of similar models which additionally adjusted for time-varying social isolation (for models of incident loneliness) or loneliness (for models for incident social isolation). For these analyses on incident social isolation or incident loneliness, the last observation was carried forward for missing follow-up data on loneliness ($n = 42$ out of 10,349 observations) and social isolation ($n = 563$ out of 12,079 observations), respectively. Sensitivity analyses were conducted using ordinal measures of loneliness [low (score of 3), moderate (score of 4–5), high (score of $\geq$6)] and social isolation [low (score of 0), moderate (score of 1), high (score of $\geq$2)]. We used $\geq$2 as our cut-off for high social isolation since our study sample included relatively few people who scored 4 or 5 (0.4 % and 0.05 % of the study sample size, respectively) and so we combined people who scored 4 or 5 with those who scored 3 (2.29 %) and 2 (11.7 %) to ensure the study was sufficiently powered to examine and significant associations. We also repeated the analyses after excluding marital status as a covariate as social isolation may be correlated with marital status. All analyses were conducted in STATA SE v17.

3. Results

A total of 17,273 eligible participants completed a baseline self-completion questionnaire between 2004/2005 and 2018/2019. Our study sample consisted of 6031 (34.9 %) participants with complete data on loneliness, social isolation, multimorbidity at baseline and at least one follow-up period and covariate data at all time points (Fig. 1). Participants in the full eligible sample were more likely widowed, had no educational qualifications, not currently in work, and had lower physical activity levels than those in our study sample (Appendix Table A1). The mean age of our study sample was 61.4 (7.8) years, 3305 (54.8 %) were female, 5880 (97.5 %) were of White ethnicity, 4573 (75.8 %) were married, and 3105 (51.5 %) were currently in work (Table 1). At baseline, 2223 (36.9 %) participants had multimorbidity,

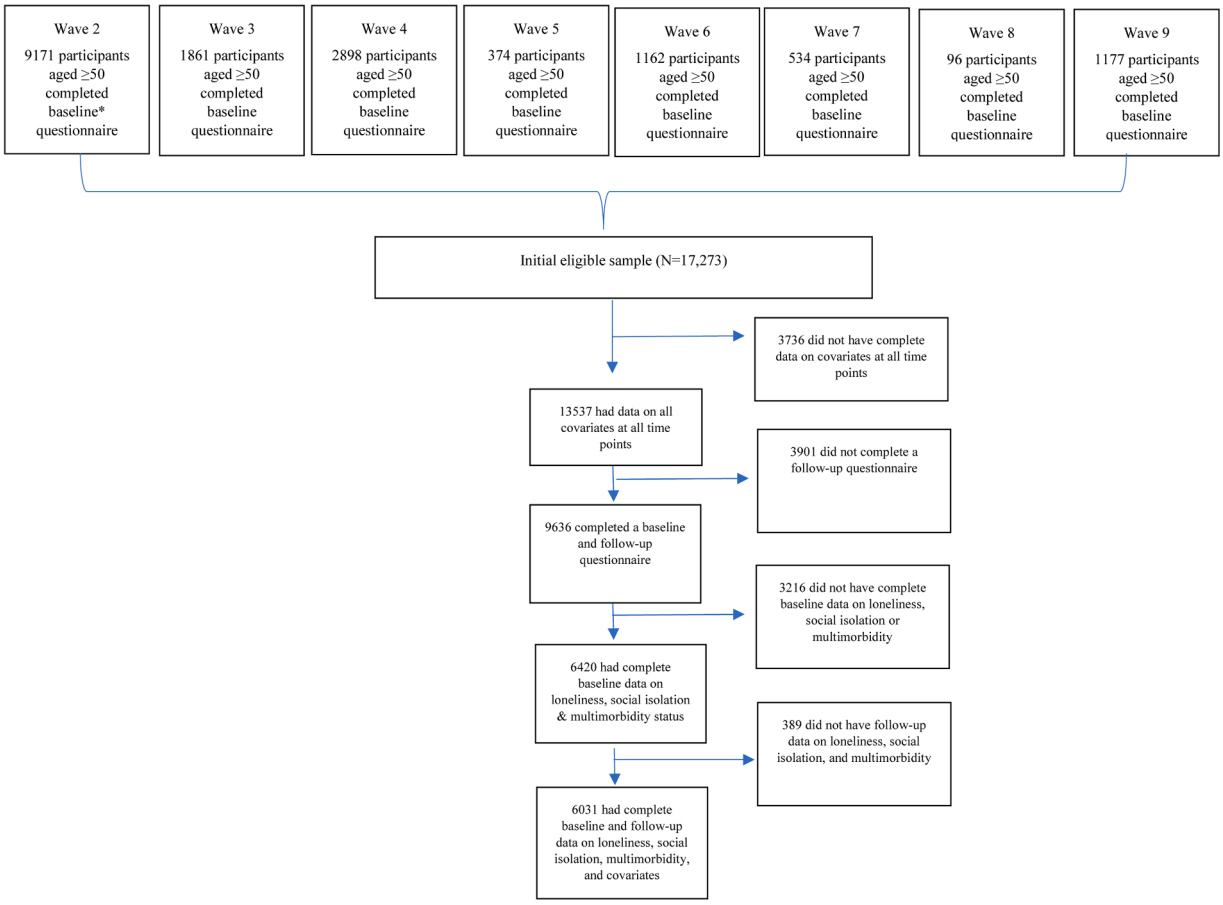

Fig. 1. Flowchart showing study sample selection for analyses on the association between multimorbidity, loneliness and social isolation.
**We defined baseline as the first wave of data collection at which a participant was aged $\geq$50 years and therefore met our eligibility criteria.

Table 1
Baseline characteristics of study sample ($n = 6031$).

Characteristic	All (n = 6031)	Multimorbidity at baseline		Loneliness at baseline		Social isolation at baseline	
		No (n = 3808)	Yes (n = 2223)	Not lonely (n = 3440)	Lonely (n = 2591)	Not socially isolated (n = 2967)	Socially isolated (n = 3064)
Mean age (SD)	61.4 (7.8)	59.9 (7.2)	63.8 (8.1)	61.7 (7.8)	60.9 (7.7)	61.3 (7.9)	61.5 (7.7)
Sex, n (%)							
Male	2726 (45.2)	1776 (46.6)	950 (42.7)	1666 (48.4)	1060 (40.9)	1323 (44.6)	1403 (45.8)
Female	3305 (54.8)	2032 (53.4)	1273 (57.3)	1774 (51.6)	1531 (59.1)	1644 (55.4)	1661 (54.2)
Ethnicity, n (%)							
White	5880 (97.5)	3711 (97.5)	2169 (97.6)	3378 (98.2)	2502 (96.6)	2900 (97.7)	2980 (97.3)
Non-white	151 (2.5)	97 (2.6)	54 (2.4)	62 (1.8)	89 (3.4)	67 (2.3)	84 (2.7)
Marital status, n (%)							
Married	4573 (75.8)	2943 (77.3)	1630 (73.3)	2851 (82.9)	1722 (66.5)	2679 (90.3)	1894 (61.8)
Single, never married	54 (0.9)	33 (0.9)	21 (0.9)	12 (0.4)	42 (1.6)	7 (0.2)	47 (1.5)
Divorced or separated	861 (14.3)	507 (13.3)	354 (15.9)	385 (11.2)	476 (18.4)	233 (7.9)	628 (20.5)
Widowed	543 (9.0)	325 (8.5)	218 (9.8)	192 (5.6)	351 (13.6)	48 (1.6)	495 (16.2)
Education, n (%)							
No qualifications	1443 (23.9)	783 (20.6)	660 (29.7)	778 (22.6)	665 (25.7)	567 (19.1)	876 (28.6)
Intermediate	2990 (49.6)	1974 (51.8)	1016 (45.7)	1705 (49.6)	1285 (49.6)	1517 (51.1)	1473 (48.1)
Degree level or higher	1143 (19.0)	819 (21.5)	324 (14.6)	716 (20.8)	427 (16.5)	671 (22.6)	472 (15.4)
Foreign/other	455 (7.5)	232 (6.1)	223 (10.0)	241 (7.1)	214 (8.3)	212 (7.2)	243 (7.9)
Socioeconomic status (NS-SEC3 classification), n (%)							
Managerial and professional occupation	2274 (37.7)	1540 (40.4)	734 (33.0)	1401 (40.7)	873 (33.7)	1271 (42.8)	1003 (32.8)
Intermediate occupation	1519 (25.2)	965 (25.3)	554 (24.9)	880 (25.6)	639 (24.7)	756 (25.5)	763 (24.9)
Routine and manual occupation	2204 (36.5)	1289 (33.9)	915 (41.2)	1147 (33.3)	1060 (40.9)	918 (30.9)	1286 (42.0)
Other	34 (0.6)	14 (0.4)	20 (0.9)	15 (0.4)	19 (0.7)	22 (0.7)	12 (0.4)
Total wealth* **(log-transformed)**	9.6 (2.7)	9.8 (2.5)	9.1 (2.9)	9.9 (2.4)	9.1 (2.9)	10.1 (2.2)	9.1 (2.9)
Currently working n (%)							
Not in work	2926 (48.5)	1453 (38.2)	1473 (66.3)	1662 (48.3)	1264 (48.8)	1413 (47.6)	1513 (49.4)
In work	3105 (51.5)	2355 (61.8)	750 (33.7)	1778 (51.7)	1327 (51.2)	1554 (52.4)	1551 (50.6)
Smoking status, n (%)							
Non-smoker	2435 (40.4)	1628 (42.8)	807 (36.3)	1385 (40.3)	1050 (40.5)	1302 (43.9)	1133 (37.0)
ex-smoker	2759 (45.8)	1662 (43.6)	1097 (49.4)	1626 (47.3)	1133 (43.7)	1381 (46.6)	1378 (45.0)
Smoker	837 (13.9)	518 (13.6)	319 (14.4)	429 (12.5)	408 (15.8)	284 (9.6)	553 (18.1)
Physical activity level, n (%)							
No activity	259 (4.3)	105 (2.8)	154 (6.9)	111 (3.2)	148 (5.7)	92 (3.1)	167 (5.5)
Mild activity	644 (10.7)	307 (8.1)	337 (15.2)	291 (8.5)	353 (13.6)	256 (8.6)	388 (12.7)
Moderate activity	2962 (49.1)	1834 (48.2)	1128 (50.7)	1711 (49.7)	1251 (48.3)	1385 (46.7)	1577 (51.5)
Vigorous activity	2166 (35.9)	1562 (41.0)	604 (27.2)	1327 (38.6)	839 (32.4)	1234 (41.6)	932 (30.4)
Alcohol consumption, n (%)							
not at all last 12months	448 (7.4)	218 (5.7)	230 (10.4)	208 (6.1)	240 (9.3)	193 (6.5)	255 (8.3)
Once/twice a year/every couple months	806 (13.4)	441 (11.6)	365 (16.4)	376 (10.9)	430 (16.6)	313 (10.6)	493 (16.1)
Once or twice a month	739 (12.3)	449 (11.8)	290 (13.1)	403 (11.7)	336 (13.0)	343 (11.6)	396 (12.9)
Once/twice a week	1675 (27.8)	1103 (29.0)	572 (25.7)	966 (28.1)	709 (27.3)	853 (28.8)	822 (26.8)
3–6 days a week	1298 (21.5)	901 (23.7)	397 (17.9)	824 (24.0)	474 (18.3)	699 (23.6)	599 (19.6)
Almost daily	1065 (17.7)	696 (18.3)	369 (16.6)	663 (19.3)	402 (15.5)	566 (19.1)	499 (16.3)
Multimorbidity, n (%)							
No	3808 (63.1)	3808 (100.0)	0 (0.0)	2310 (67.2)	1498 (57.8)	1930 (65.1)	1878 (61.3)
Yes	2223 (36.9)	0 (0.0)	2223 (100.0)	1130 (32.9)	1093 (42.2)	1037 (35.0)	1186 (38.7)
Loneliness, n (%)							
Low	3440 (57.0)	2310 (60.7)	1130 (50.8)	3440 (100.0)	0 (0.0)	1942 (65.5)	1498 (48.9)
Medium/High	2591 (43.0)	1498 (39.3)	1093 (49.2)	0 (0.0)	2591 (100.0)	1025 (34.6)	1566 (51.1)
Social isolation, n (%)							
Low	2967 (49.2)	1930 (50.7)	1037 (46.7)	1942 (56.5)	1025 (39.6)	2967 (100.0)	0 (0.0)
Medium/High	3064 (50.8)	1878 (49.3)	1186 (53.4)	1498 (43.6)	1566 (60.4)	0 (0.0)	3064 (100.0)

* Total wealth was the total financial wealth (savings + investments but not subtracting any financial debt). Some total values may be greater than 100 % due to rounding up.

2591 (43.0 %) were classed as lonely, and 3064 (50.8 %) were classed as socially isolated. One thousand five hundred and sixty-six (26.0 %) were classed as 'lonely and socially isolated', 1025 (17.0 %) were classed as 'lonely and not socially isolated', 1498 (24.8 %) were classed as 'not lonely and socially isolated', and 1942 (32.2 %) were classed as 'not lonely, not socially isolated'. Appendix Table A2 shows the distribution of responses for each item of loneliness and social isolation at baseline.

Participants who were lonely at baseline were more likely female, unmarried, had lower educational qualifications and socioeconomic status, less physically active, consumed lower amounts of alcohol over the last 12 months and had multimorbidity compared to participants who were not lonely at baseline (Table 1). Participants who were socially isolated at baseline were more likely unmarried, had lower educational qualifications and socioeconomic status, current smokers, were less physically active, consumed lower amounts of alcohol over the last 12 months and had multimorbidity. Compared to participants without multimorbidity at baseline, participants with multimorbidity at baseline were more likely older, female, unmarried, had lower educational qualification and socioeconomic status, not currently in work, less physically active, consumed lower amounts of alcohol over the last 12 months, lonely and socially isolated (Table 1). Appendix Table A3 presents participant characteristics for each ordinal category of loneliness

and social isolation.

Our analytical sample for the association of loneliness and social isolation with risk of incident multimorbidity consisted of 3808 (63.1 %) participants who did not have multimorbidity at baseline. During a median follow-up of 8 (IQR: 2–12) years, 1281 (33.6 %) participants developed multimorbidity. Table 2 presents the unadjusted and adjusted HR for risk of incident multimorbidity. In the fully-adjusted models (adjusting for loneliness or social isolation, all demographic and health behaviour variables), loneliness was significantly associated with increased risk of incident multimorbidity [adjusted HR (95 % CI): 1.38 (1.15–1.65)]. In fully-adjusted models, social isolation was not significantly associated with risk of incident multimorbidity [aHR (95 % CI): 0.97 (0.81–1.16)]. Table 3 presents the unadjusted and adjusted HR for risk of incident multimorbidity when the models were repeated using ordinal categories of loneliness and social isolation. Compared to participants with low levels of loneliness, participants with high levels of loneliness had higher risk of incident multimorbidity [aHR (95 % CI):1.71 (1.32–2.21)] in fully-adjusted models (adjusting for social isolation status, all demographic variables and all health behaviour variables) (Table 3). Compared to participants with low levels of social isolation, participants with high levels of social isolation did not have higher risk of incident multimorbidity [aHR (95 % CI):1.16 (0.88–1.52)] in fully-adjusted models (adjusting for loneliness status, all demographic variables and all health behaviour variables) (Table 3).

Our analytical sample for the association of multimorbidity with risk of incident loneliness consisted of 3440 (57.0 %) participants who did not feel lonely at baseline. The median follow-up was 8 (IQR: 2–12) years, during which 1458 (42.4 %) participants reported loneliness. Table 4 presents the unadjusted and adjusted HR for risk of incident loneliness. In the fully-adjusted models, multimorbidity was significantly associated with increased risk of incident loneliness [aHR (95 % CI): 1.55 (1.30–1.84)].

Our analytical sample for the association of multimorbidity with risk of incident social isolation consisted of 2967 (49.2 %) participants who were not socially isolated at baseline (Table 1). The median follow-up was 6 (IQR: 2–12) years during which 1419 (47.8 %) participants reported being socially isolated. In fully-adjusted models, multimorbidity was not significantly associated with risk of incident social isolation [HR (95 % CI): 1.09 (0.92–1.28)] (Table 4).

Additional regression models excluding marital status as a covariate yielded consistent results (Appendix Table A4). In these models, socially isolated participants did not have higher risk of incident multimorbidity [aHR (95 % CI): 0.99 (0.82–1.18)]. Similarly, participants with multimorbidity did not have higher risk of incident social isolation [aHR (95 % CI): 1.08 (0.91–1.27)].

4. Discussion

In this population-based study of adults aged ≥50 years, we found a statistically significant bidirectional association between loneliness and multimorbidity. Loneliness (particularly high levels of loneliness) was associated with an increased risk of multimorbidity up to 14 years later, and multimorbidity was associated with an increased risk of loneliness up to 14 years later. Demographic and health behaviour variables did not explain this increased risk and consistent results were obtained using ordinal measures of loneliness. We did not find a significant prospective longitudinal association between social isolation and multimorbidity in this cohort.

To our knowledge, this is the first study to examine a bidirectional association between multimorbidity, loneliness and social isolation. Pengpid and Peltzer (2023) assessed the association between multimorbidity and incident and persistent loneliness two years later in a sample of 3696 adults living in Thailand and found that multimorbidity was associated with increased risk of loneliness. Using data from adults aged 50 years old in the Survey on Health, Ageing and Retirement in Europe (SHARE) study, Sieber et al. (2023) found that multimorbidity was associated with increased risk of loneliness two years later. Our findings are also consistent with an existing panel study that assessed associations over time using measures of loneliness and multimorbidity over multiple time periods and reported that changes in multimorbidity were associated with increases in loneliness over four years in adults living in Germany (Schübbe et al., 2023). Similarly, our findings are consistent with a UK Biobank study that reported a significant association between loneliness and cardiometabolic multimorbidity (Xiao et al., 2024). In contrast, Hajek et al. reported that changes in number of conditions was not significantly associated with changes in loneliness over six years in sample of adults from the SHARE study (Hajek & König, 2020). Using data from twelve years of the SHARE study, Cantarero-Prieto et al. found that social participation was significantly associated with lower risk of multimorbidity (Cantarero-Prieto et al., 2018). A UK study also found small social network size was associated with incident multimorbidity among UK working-age adults (Stagg et al., 2023). Differences in measures (for example number of conditions rather than a binary indicator of multimorbidity and social participation rather than social isolation) and analytical models used could explain the discrepant findings. Our study extends the current literature on this topic by being first to demonstrate the bidirectional nature of the association of multimorbidity with both loneliness and social isolation.

The finding that loneliness was significantly prospectively associated with multimorbidity (and vice versa), while social isolation was not, may be expected as loneliness and social isolation are thought to be only weakly to moderately correlated (Coyle & Dugan, 2012). This finding is also in line with previous research that has suggested that subjective experiences of social connection may be more strongly linked to risk of single diseases such as cardiovascular disease or depression (Bu et al., 2020; M Elovainio et al., 2023). Loneliness may influence development of multimorbidity through increased feelings of stress and associated inflammation (Hawkley & Cacioppo, 2010; Walker et al., 2019). Perceived stress has been linked to higher risk of multimorbidity (Prior et al., 2017) and loneliness may be linked to poor regulation of inflammation (Walker et al., 2019). In contrast, a meta-analysis of studies on the association of inflammation with loneliness and social

Table 2
Association of risk of incident multimorbidity with loneliness and social isolation.

	Model 1		Model 2		Model 3		Model 4	
	HR (95 % CI)	p-value	HR (95 % CI)	p-value	HR (95 % CI)	p-value	HR (95 % CI)	p-value
Loneliness								
Not lonely (ref)	1		1		1		1	
Lonely	**1.40 (1.17–1.67)**	**<0.001**	**1.38 (1.15–1.65)**	**<0.001**	**1.39 (1.16–1.66)**	**<0.001**	**1.38 (1.15–1.65)**	**<0.001**
Social isolation								
Not socially isolated (ref)	1		1		1		1	
Socially isolated	1.14 (0.96–1.35)	0.144	1.08 (0.90–1.29)	0.399	0.99 (0.82–1.18)	0.885	0.97 (0.81–1.16)	0.745

Model 1: unadjusted model including only loneliness or social isolation. Model 2: model including loneliness and social isolation. Model 3: Model 2 + demographics (age, sex, ethnicity, marital status, socioeconomic status and education status). Model 4: Model 3 + health behaviour variables (smoking status, alcohol consumption and physical activity).

Table 3
Association of risk of incident multimorbidity with ordinal categories of loneliness and social isolation.

	Model 1		Model 2		Model 3		Model 4	
	HR (95 % CI)	p-value	HR (95 % CI)	p-value	HR (95 % CI)	p-value	HR (95 % CI)	p-value
Loneliness level								
Low (ref)	1		1		1		1	
Moderate	1.22 (1.00–1.50)	0.051	1.20 (0.97–1.47)	0.090	1.22 (0.99–1.50)	0.061	1.22 (0.99–1.49)	0.063
High	**1.79 (1.39–2.30)**	**<0.001**	**1.73 (1.34–2.23)**	**<0.001**	**1.73 (1.33–2.24)**	**<0.001**	**1.71 (1.32–2.21)**	**<0.001**
Social isolation level								
Low (ref)	1		1		1		1	
Moderate	1.02 (0.84–1.24)	0.835	0.97 (0.80–1.17)	0.733	0.91 (0.75–1.11)	0.336	0.90 (0.74–1.09)	0.287
High	**1.49 (1.16 −1.93)**	**0.002**	**1.36 (1.04–1.76)**	**0.022**	1.19 (0.91–1.57)	0.203	1.16 (0.88–1.52)	0.296

Model 1: unadjusted model including only loneliness or social isolation. Model 2: model including loneliness and social isolation. Model 3: Model 2 + demographics (age, sex, ethnicity, marital status, socioeconomic status and education status). Model 4: Model 3 + health behaviour variables (smoking status, alcohol consumption and physical activity).

Table 4
Association of multimorbidity with risk of incident loneliness (n = 3440) and risk of incident social isolation (n = 2967).

	Model 1		Model 2		Model 3		Model 4	
	HR (95 % CI)	p-value	HR (95 % CI)	p-value	HR (95 % CI)	p-value	HR (95 % CI)	p-value
Incident loneliness								
Multimorbidity								
No (ref)	1		1		1		1	
Yes	**1.51 (1.28–1.79)**	**<0.001**	**1.51 (1.27–1.79)**	**<0.001**	**1.58 (1.33–1.88)**	**<0.001**	**1.55 (1.30–1.84)**	**<0.001**
Incident social isolation								
Multimorbidity								
No (ref)	1		1		1		1	
Yes	1.08 (0.92–1.27)	0.341	1.08 (0.91–1.27)	0.374	1.10 (0.93–1.30)	0.248	1.09 (0.92–1.28)	0..334

Model 1: unadjusted model. Model 2: Model 1 + social isolation or loneliness. Model 3: Model 2 + demographics (age, sex, ethnicity, marital status, socioeconomic status and education status). Model 4: Model 3 + health behaviour variables (smoking status, alcohol consumption and physical activity).

isolation found loneliness was linked to inflammatory markers (e.g.: interleukin-6) whereas social isolation was not (Smith et al., 2020, May)."

We did not find a significant association between social isolation and multimorbidity. This finding suggests that it is the quality and perception of support from social connection that is important for development of multimorbidity, rather than the structural aspect (frequency of contact or size of network). This finding is in line with other studies (M Elovainio et al., 2023; Rafnsson et al., 2020) that have used a similar measure of social isolation and reported that loneliness but not social isolation is linked to single conditions. We may have observed a significant association with multimorbidity if we used a measure of social isolation that captures perceived support and quality of relationships (for example the Lubben Social Network Scale (LSNS-6)); some cross-sectional studies using LSNS reported significant associations with multimorbidity, while studies using a measure that focused on frequency of social contact did not (Hounkpatin et al., 2024). Our finding of a lack of association between social isolation and multimorbidity may be due to the specific conditions assessed in the study or the use of broad categories of conditions. Previous studies have reported differential associations of loneliness and social isolation with specific health outcomes (Hong et al., 2023). Social isolation has been found to be a strong predictor of cognitive impairment and other functional limitations (e.g.: hearing or vision loss) (Hong et al., 2023). We have not captured these health outcomes in our study as the ELSA survey did not ask participants about whether they had been diagnosed (by a doctor) with these health conditions.

Our finding that loneliness was a risk factor and outcome associated with multimorbidity independent of social isolation status highlights the importance of identifying and reducing loneliness, including in people who may have existing social connections. Interventions aimed at reducing loneliness may facilitate more meaningful and deeper relationships. Management of multimorbidity also needs to consider loneliness. Further research exploring mechanisms underlying this bidirectional relationship can further inform interventions.

Strengths of our study include the large population-based sample, long follow-up period and availability of measures (including important confounders and validated measures of loneliness) over multiple years. There are important limitations to this study. First, the survey uses self-report data which may be susceptible to recall and social desirability bias. Secondly, we are not able to make any causal inferences about the associations presented here. While we were able to adjust for several confounders, there may be unobserved heterogeneity or additional confounders we weren't able to adjust. Third, we used complete case data and excluded people who did not have complete data on loneliness, social isolation and multimorbidity at baseline and at least one follow-up period. Fourth, we derived a measure of social isolation based on previous studies assessing social isolation in the ELSA dataset, it is unclear whether similar results would be obtained using other validated measures such as the 6-item Lubben Social Network Scale (LSNS-6). Fifth, we defined multimorbidity based on whether participants had ever been diagnosed with a condition; it is possible that some of these conditions may have resolved which was not accounted for in our analyses. Finally, our results are generalisable to the national English population but may not extend to other countries, for example with larger proportion of ethnic minorities as our study sample included very few people of non-white ethnicity.

In conclusion, this study provides evidence for a bidirectional association between multimorbidity and loneliness in older adults in England. Interventions focused on addressing the antecedents of loneliness may prevent or delay the development of multimorbidity and improve wellbeing for people living with multimorbidity. However, such interventions may focus on helping people build meaningful connections and addressing factors that impact this, rather than broadening social networks.

5. Contributors

HH designed the study, with input from MS,AF, HDM, BS, NI. HH analysed the data and drafted the first version of the manuscript. NI supervised the data analyses, verified the data and analyses, and revised the manuscript. BS provided advice on the statistical analysis and revised the manuscript. HH, BS, NI, MS, AF, HDM revised the manuscript and approved the final version for submission for publication.

6. Data sharing

The English Longitudinal Study of Ageing (ELSA) data can be publicly accessed through UK Data Service portal. Data and supporting documents are available from: https://www.elsa-project.ac.uk/accessing-elsa-data

CRediT authorship contribution statement

Hilda Hounkpatin: Writing – review & editing, Writing – original draft, Visualization, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Nazrul Islam:** Writing – review & editing, Supervision, Methodology. **Beth Stuart:** Writing – review & editing, Methodology. **Miriam Santer:** Writing – review & editing, Supervision, Methodology. **Andrew Farmer:** Writing – review & editing, Supervision. **Hajira Dambha-Miller:** Writing – review & editing, Supervision, Methodology.

Declaration of competing interest

None.

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Appendix

Tables A1–A4.

Table A1
Comparison of baseline characteristics of study sample and full sample.

Characteristic	Study sample (n = 6031)	Full sample (n = 17,273)*
Mean age (SD)	61.4 (7.8)	62.2 (10.3)
Sex, n (%)		
Male	2726 (45.2)	7932 (45.9)
Female	3305 (54.8)	9338 (54.1)
Ethnicity, n (%)		
White	5880 (97.5)	16,499 (95.8)
Non-white	151 (2.5)	730 (4.2)
Marital status, n (%)		
Married	4573 (75.8)	10,760 (63.9)
Single, never married	54 (0.9)	1196 (7.1)
Divorced or separated	861 (14.3)	2328 (13.8)
Widowed	543 (9.0)	2545 (15.1)
Education, n (%)		
No qualifications	1443 (23.9)	5165 (31.1)
Intermediate	2990 (49.6)	7498 (45.1)
Degree level or higher	1143 (19.0)	2736 (16.5)
Foreign/other	455 (7.5)	1212 (7.3)
Socioeconomic status (NS-SEC3 classification), n (%)		
Managerial and professional occupation	2274 (37.7)	5073 (33.2)
Intermediate occupation	1519 (25.2)	3657 (23.9)
Routine and manual occupation	2204 (36.5)	6345 (41.5)
Other	34 (0.6)	198 (1.3)
Total wealth (log-transformed)	9.6 (2.7)	9.0 (3.1)
Currently working, n (%)		
Not in work	2926 (48.5)	8916 (51.6)
In work	3105 (51.5)	8357 (48.4)
Smoking status		
Non-smoker	2435 (40.4)	6694 (39.8)
ex-smoker	2759 (45.8)	7287 (43.3)
Smoker	837 (13.9)	2840 (16.9)
Physical activity level, n (%)		
No activity	259 (4.3)	1379 (8.1)
Mild activity	644 (10.7)	2419 (14.1)
Moderate activity	2962 (49.1)	7959 (46.4)
Vigorous activity	2166 (35.9)	5382 (31.4)
Alcohol consumption, n (%)		
Not at all last 12 months	448 (7.4)	1396 (10.6)
Once/twice a year/every couple months	806 (13.4)	2049 (15.6)
Once or twice a month	739 (12.3)	1554 (11.8)

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Table A1 (*continued*)

Characteristic	Study sample (n = 6031)	Full sample (n = 17,273)*
Once/twice a week	1675 (27.8)	3392 (25.8)
3–6 days a week	1298 (21.5)	2557 (19.4)
Almost daily	1065 (17.7)	2211 (16.8)
Multimorbidity, n (%)		
No	3808 (63.1)	10,544 (61.2)
Yes	2223 (36.9)	6693 (38.8)
Loneliness, n (%)		
Low	3440 (57.0)	7260 (51.7)
Medium/High	2591 (43.0)	6791 (48.3)
Social isolation, n (%)		
Low	2967 (49.1)	4088 (42.8)
Medium/High	3074 (50.9)	5456 (57.2)

* Number of people with data on sex, ethnicity, marital status, education, socioeconomic status, total wealth, smoking status, physical activity, alcohol consumption, loneliness, and social isolation was 17,270, 17,229, 16,829, 16,611, 15,273, 16,888, 16,821, 17,139, 13,159, 14,051, and 9544.

Table A2
Summary of responses for individual items or categories of loneliness and social isolation.

	Possible responses			**Median score (IQR)**
	Hardly ever or never (score=1)	Some of the time (score=2)	Often (score=3)	
Loneliness item				
How often feels they lack companionship	2837 (74.4)	851 (22.3)	126 (3.3)	1 (1–3)
How often feels left out	2752 (72.2)	985 (25.8)	77 (2.0)	1 (1–3)
How often feels isolated from others	2954 (77.5)	783 (20.5)	77 (2.0)	1(1–3)
Total loneliness score (sum of above 3)				3(3–9)
	No (0)	Yes (1)		
Social isolation				
Not being married or cohabitating	3334 (87.6)	474 (12.5)		0 (0–1)
Having less than monthly face-to-face, telephone or written/e-mail contact with children outside the household	3686 (96.8)	1222(3.2)		0 (0–1)
Less than monthly contact with other relatives outside the household	3069 (80.6)	739 (19.4)		0 (0–1)
Less than monthly contact with friends	3473 (91.2)	335 (8.8)		0 (0–1)
Not being a member in any civic organisations	2980 (78.3)	828 (21.7)		0 (0–1)
Total social isolation score				0(0–4)

This table shows that for each item of loneliness, most participants scored low. Similarly, for each item of social isolation, most participants scored low. Total scores for loneliness ranged from the minimum score of 3 to maximum score of 9 (median=3). Scores for social isolation ranged from minimum score of 0 to 4 (median=0 and there were no scores of 5).

Table A3
Summary characteristics of participants by loneliness and social isolation ordinal category at baseline.

	Multimorbidity at baseline			Loneliness level at baseline			Social isolation at baseline		
Characteristic	All (n = 6031)	No (n = 3808)	Yes (n = 2223)	Low (n = 3440)	Moderate (n = 1660)	High(n = 931)	Low (n = 2967)	Moderate (n = 2192)	High (n = 872)
Mean age (SD)	61.4 (7.8)	59.9 (7.2)	63.8 (8.1)	61.7 (7.8)	61.1 (7.8)	60.5 (7.5)	61.3 (7.9)	61.5 (7.7)	61.3 (7.7)
Sex, n (%)									
Male	2726 (45.2)	1776 (46.6)	950 (42.7)	1666 (48.4)	709 (42.7)	351 (37.7)	1323 (44.6)	958 (43.7)	445 (51.0)
Female	3305 (54.8)	2032 (53.4)	1273 (57.3)	1774 (51.6)	951 (57.3)	580 (62.3)	1644 (55.4)	1234 (56.3)	427 (49.0)
Ethnicity, n (%)									
White	5880 (97.5)	3711 (97.5)	2169 (97.6)	3378 (98.2)	1607 (96.8)	895 (96.1)	2900 (97.7)	2135 (97.4)	845 (96.9)
Non-white	151 (2.5)	97 (2.6)	54 (2.4)	62 (1.8)	53 (3.2)	36 (3.9)	67 (2.3)	57 (2.6)	27 (3.1)
Marital status, n (%)									
Married	4573 (75.8)	2943 (77.3)	1630 (73.3)	2851 (82.9)	1188 (71.6)	534 (57.4)	2679 (90.3)	1483 (67.7)	411 (47.1)
Single, never married	54 (0.9)	33 (0.9)	21 (0.9)	12 (0.4)	21 (1.3)	21 (2.3)	7 (0.2)	24 (1.1)	23 (2.6)
Divorced or separated	861 (14.3)	507 (13.3)	354 (15.9)	385 (11.2)	279 (16.8)	197 (21.2)	233 (7.9)	385 (17.6)	243 (27.9)
Widowed	543 (9.0)	325 (8.5)	218 (9.8)	192 (5.6)	172 (10.4)	179 (19.2)	48 (1.6)	300 (13.7)	195 (22.4)
Education, n (%)									
No qualifications	1443 (23.9)	783 (20.6)	660 (29.7)	778 (22.6)	412 (24.8)	253 (27.2)	567 (19.1)	599 (27.3)	277 (31.8)
Intermediate	2990 (49.6)	1974 (51.8)	1016 (45.7)	1705 (49.6)	828 (49.9)	457 (49.1)	1517 (51.1)	1048 (47.8)	425 (48.7)

(*continued on next page*)

Table A3 (*continued*)

Characteristic	Multimorbidity at baseline			Loneliness level at baseline			Social isolation at baseline		
	All (n = 6031)	No (n = 3808)	Yes (n = 2223)	Low (n = 3440)	Moderate (n = 1660)	High(n = 931)	Low (n = 2967)	Moderate (n = 2192)	High (n = 872)
Degree level or higher	1143 (19.0)	819 (21.5)	324 (14.6)	716 (20.8)	278 (16.8)	149 (16.0)	671 (22.6)	369 (16.8)	103 (11.8)
Foreign/other	455 (7.5)	232 (6.1)	223 (10.0)	241 (7.01)	142 (8.6)	72 (7.7)	212 (7.2)	176 (8.0)	67 (7.7)
Socioeconomic status (NS-SEC3 classification), n (%)									
Managerial and professional occupation	2274 (37.7)	1540 (40.4)	734 (33.0)	1401 (40.7)	584 (35.2)	289 (31.0)	1271 (42.8)	750 (34.2)	253 (29.0)
Intermediate occupation	1519 (25.2)	965 (25.3)	554 (24.9)	880 (25.6)	415 (25.0)	224 (24.1)	756 (25.5)	548 (25.0)	215 (24.7)
Routine and manual occupation	2204 (36.5)	1289 (33.9)	915 (41.2)	1144 (33.3)	654 (39.4)	406 (43.6)	918 (30.9)	886 (40.4)	400 (45.9)
Other	34 (0.6)	14 (0.4)	20 (0.9)	15 (0.4)	7 (0.4)	12 (1.3)	22 (0.7)	8 (0.4)	4 (0.5)
Total wealth* (log-transformed)	9.6 (2.7)	9.8 (2.5)	9.1 (2.9)	9.9 (2.4)	9.4 (2.8)	8.8 (3.1)	10.1 (2.2)	9.4 (2.8)	8.3 (3.2)
Currently working n (%)									
Not in work	2926 (48.5)	1453 (38.2)	1473 (66.3)	1662 (48.3)	793 (47.8)	471 (50.6)	1413 (47.6)	1077 (49.1)	436 (50.0)
In work	3105 (51.5)	2355 (61.8)	750 (33.7)	1778 (51.7)	867 (52.2)	460 (49.4)	1554 (52.4)	1115 (50.9)	436 (50.0)
Smoking status, n (%)									
Non-smoker	2435 (40.4)	1628 (42.8)	807 (36.3)	1385 (40.3)	682 (41.1)	368 (39.5)	1302 (43.9)	860 (39.2)	273 (31.3)
ex-smoker	2759 (45.8)	1662 (43.6)	1097 (49.4)	1626 (47.3)	725 (43.7)	408 (43.8)	1381 (46.6)	986 (45.0)	392 (45.0)
Smoker	837 (13.9)	518 (13.6)	319 (14.4)	429 (12.5)	253 (15.2)	155 (16.7)	284 (9.6)	346 (15.8)	207 (23.7)
Physical activity level, n (%)									
No activity	259 (4.3)	105 (2.8)	154 (6.9)	111 (3.2)	88 (5.3)	60 (6.4)	92 (3.1)	106 (4.8)	61 (7.0)
Mild activity	644 (10.7)	307 (8.1)	337 (15.2)	291 (8.5)	223 (13.4)	130 (14.0)	256 (8.6)	262 (12.0)	126 (14.5)
Moderate activity	2962 (49.1)	1834 (48.2)	1128 (50.7)	1711 (49.7)	801 (48.3)	450 (48.3)	1385 (46.7)	1119 (51.1)	458 (52.5)
Vigorous activity	2166 (35.9)	1562 (41.0)	604 (27.2)	1327 (38.6)	548 (33.0)	291 (31.3)	1234 (41.6)	705 (32.2)	227 (26.0)
Alcohol consumption, n (%)									
not at all last 12months	448 (7.4)	218 (5.7)	230 (10.4)	208 (6.1)	140 (8.4)	100 (10.7)	193 (6.5)	166 (7.6)	89 (10.2)
Once/twice a year/every couple months	806 (13.4)	441 (11.6)	365 (16.4)	376 (10.9)	244 (14.7)	186 (20.0)	313 (10.6)	317 (14.5)	176 (20.2)
Once or twice a month	739 (12.3)	449 (11.8)	290 (13.1)	403 (11.7)	220 (13.3)	116 (12.5)	343 (11.6)	300 (13.7)	96 (11.0)
Once/twice a week	1675 (27.8)	1103 (29.0)	572 (25.7)	966 (28.1)	461 (27.8)	248 (26.6)	853 (28.8)	618 (28.2)	204 (23.4)
3–6 days a week	1298 (21.5)	901 (23.7)	397 (17.9)	824 (24.0)	324 (19.5)	150 (16.1)	699 (23.6)	445 (20.3)	154 (17.7)
Almost daily	1065 (17.7)	696 (18.3)	369 (16.6)	663 (19.3)	271 (16.3)	131 (14.1)	566 (19.1)	346 (15.8)	153 (17.6)
Multimorbidity, n (%)									
No	3808 (63.1)	3808 (100.0)	0 (0.0)	2310 (67.2)	989 (59.6)	509 (54.7)	1930 (65.1)	1360 (62.0)	518 (59.4)
Yes	2223 (36.9)	0 (0.0)	2223 (100.0)	1130 (32.9)	671 (40.4)	422 (45.3)	1037 (35.0)	832 (38.0)	354 (40.6)
Loneliness, n (%)									
Low	3440 (57.0)	2310 (60.7)	1130 (50.8)	3440 (100.0)	0 (0)	0 (0)	1942 (65.5)	1134 (51.7)	651 (74.7)
1660 (27.5)	989 (26.0)	671 (30.2)	0 (0.0)	1660 (100.0)	0(0)	714 (24.1)	659 (30.1)		
High	931 (15.4)	509 (13.4)	422 (19.0)	0 (0)	0 (0)	931 (100.0)	311 (10.5)	399 (18.2)	221 (25.3)
Social isolation, n (%)									
Low	2967 (49.2)	1930 (50.7)	1037 (46.7)	1942 (56.5)	714 (43.0)	710 (76.3)	2967 (100.0)	0 (0)	0 (0)
2192 (36.4)	1360 (35.7)	832 (37.4)	1134 (33.0)	659 (39.7)	0 (0)	0 (0)	2192 (100.0)	0 (0)	
High	872 (14.5)	518 (13.6)	354 (15.9)	364 (10.6)	287 (17.3)	221 (23.7)	0 (0)	0 (0)	872 (100.0)

Table A4
Associations of multimorbidity, loneliness and social isolation over time, in models excluding marital status as a covariate.

	Model 1 HR (95 % CI)	p-value	Model 2 HR (95 % CI)	p-value	Model 3 HR (95 % CI)	p-value	Model 4 HR (95 % CI)	p-value
Incident multimorbidity								
Loneliness								
Not lonely (ref)	1		1		1		1	
Lonely	**1.40 (1.17–1.67)**	**<0.001**	**1.38 (1.15–1.65)**	**<0.001**	**1.40 (1.17–1.67)**	**<0.001**	**1.39 (1.16–1.66)**	**<0.001**
Social isolation								
Not socially isolated (ref)	1		1		1		1	
Socially isolated	1.14 (0.96–1.35)	0.144	1.08 (0.90–1.29)	0.399	1.00 (0.84–1.20)	0.965	0.99 (0.82–1.18)	0.876
Incident loneliness								
Multimorbidity								
No (ref)	1		1		1		1	
Yes	**1.51 (1.28–1.79)**	**<0.001**	**1.51 (1.27–1.79)**	**<0.001**	**1.58 (1.33–1.89)**	**<0.001**	**1.55 (1.30–1.84)**	**<0.001**
Incident social isolation								
Multimorbidity								
No (ref)	1		1		1		1	
Yes	1.08 (0.92–1.27)	0.341	1.08 (0.91–1.27)	0.374	1.10 (0.93–1.29)	0.278	1.08 (0.91–1.27)	0.373

Model 1: unadjusted model. Model 2: Model 1 + social isolation or loneliness. Model 3: Model 2 + demographics (age, sex, ethnicity, marital status, socioeconomic status and education status). Model 4: Model 3 + health behaviour variables (smoking status, alcohol consumption and physical activity).

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