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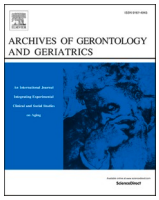

Review

Multiple long-term conditions, loneliness and social isolation: A scoping review of recent quantitative studies

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HIGHLIGHTS

- Multiple long-term conditions are associated with loneliness and social isolation.
- This association may vary for the oldest old and ethnic minorities.
- Further studies are needed to better understand this association.

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ABSTRACT

Background: Multiple long-term conditions (MLTC), loneliness and social isolation are common in older adults. Recent studies have explored the association of MLTC with loneliness and social isolation. This scoping review aimed to map this current evidence and identify gaps in the literature.
Methods: A scoping review was conducted following the PRISMA guidelines for scoping reviews. Ovid Medline, Embase, CINAHL, The Cochrane Library, PsycInfo, and Bielefeld Academic Search Engine were searched for studies published between January 2020-April 2023. Quantitative studies, published in any language, that assessed the association of MLTC with loneliness and/or social isolation were included.
Results: 1827 records were identified and screened. Of these, 17 met inclusion criteria. Most studies were cross-sectional and based on older adults. Studies were conducted in Europe, the US, Canada, and low- and middle-income countries. Ten studies focused on the association between MLTC and loneliness, six assessed the association between MLTC and social isolation and one examined associations with both loneliness and social isolation. Most studies reported a significant cross-sectional association of MLTC with loneliness, but there was weaker evidence for a longitudinal association between MLTC and loneliness and an association between MLTC and social isolation. Studies were heterogenous in terms of measures and definitions of loneliness/social isolation and MLTC, confounders adjusted for, and analytical models used, making comparisons difficult.
Conclusions: Further population-based longitudinal studies using consistent measures and methodological approaches are needed to improve understanding of the association of MLTC with both loneliness and social isolation.

1. Introduction

Multiple long-term conditions (MLTC) is commonly defined as the co-existence of two or more long-term conditions in an individual (The Academy of Medical Sciences, 2018). These long-term conditions can include physical or mental health conditions (e.g.: diabetes, depression, schizophrenia), ongoing conditions (e.g.: learning disability), symptom complexes (e.g.: chronic pain, frailty), sensory impairment (sight or hearing loss), alcohol or substance abuse (National Institute for Health Research (NIHR) 2021). MLTC continues to be one of the greatest challenges to health and social care services (Pearson-Stuttard et al., 2019). MLTC is associated with increased mortality, reduced quality of life, worse health outcomes and higher health and social care costs (Cassell et al., 2018; Soley-Bori et al., 2020; Stokes et al., 2021). MLTC is

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more prevalent in older adults, with more than 50 % of the global population of adults aged ≥60 years living with MLTC (Chowdhury et al., 2023; MacRae et al., 2023).

A growing body of research has highlighted multiple factors that contribute to the development of MLTC (Skou et al., 2022). These include biological, socioeconomic, psychosocial and behavioural determinants. In recent years, there has been an increasing interest in the role of 'emerging' lifestyle factors, such as low levels of social connection, as potentially modifiable factors that may be targeted to prevent or delay development of MLTC (Singer et al., 2019; Skou et al., 2022). Older adults are particularly vulnerable to experiencing loneliness and social isolation due to changes in their life circumstances (for example, loss of loved ones, retirement, poorer health and mobility) (Fakoya et al., 2020; Victor & Yang, 2012). Loneliness (the subjective distressing feeling of alienation that occurs when there is a significant discrepancy between one's actual and desired social relationships) and social isolation (an objective measure of inadequate social network size and lack of (or limited) social contact) have both been linked to development of long-term conditions (Cantarero-Prieto et al., 2018; Sundström et al., 2020). Loneliness and social isolation are now recognised as distinct constructs with only weak to moderate correlation with one another (Coyle & Dugan, 2012). This may be expected as social isolation refers to the structural aspect of social relationships (i.e., the existence of connections with others) while loneliness represents the functional aspect of social relationships (i.e., connections that result in perceived support and inclusion giving one a *sense* of connection) (National Academies of Sciences, Engineering & Medicine, 2020). Loneliness and social isolation have been found to have independent but differential effects on various health outcomes (Hong et al., 2023). Studies have reported larger effect sizes for the association of all-cause and cancer mortality with social isolation compared to loneliness (Hong et al., 2023; Wang et al., 2023). Social isolation has also been found to be associated with higher risk of stroke, cognitive impairment, and cardiovascular-related mortality, while loneliness has been associated with higher risk of lung disease, pain, and self-rated health (Hong et al., 2023; Wang et al., 2023). A recent study has also reported that loneliness is a stronger predictor of psychological outcomes (including depression, life satisfaction) than social isolation (Hong et al., 2023). These findings suggest social isolation and loneliness may relate to health through different pathways and both constructs need to be examined when assessing associations with MLTC.

While extensive research has examined the link between single health outcomes with loneliness and/or social isolation, fewer studies have examined their association with MLTC (Calderón-Larrañaga et al., 2018; Olaya et al., 2017). A systematic review published in 2020 identified only eight studies on the association of MLTC with loneliness or social isolation (Hajek et al., 2020). The review found some evidence for a significant association between MLTC and loneliness and a lack of studies assessing the association between MLTC and social isolation. Furthermore, there were a lack of studies exploring the direction of the link between MLTC and loneliness and mechanisms underpinning this association, which is important from an intervention perspective. Since the previous systematic review (Hajek et al., 2020) was published in 2020, additional studies have explored the link between MLTC, loneliness and social isolation, which may have addressed these limitations. Given the rapidly growing literature on this topic, the heterogeneous nature of existing studies, and the current focus on improving understanding of psychosocial determinants of MLTC in order to improve health and care outcomes for patients (National Institute of Health Research, 2020; The Academy of Medical Sciences, 2018), it is important to collectively examine these existing studies to better understand gaps in current knowledge and guide further research on this topic.

Scoping reviews are a useful method to examine all the available evidence on an emerging topic. A scoping review aims to summarise the evidence (what is known on the topic and the nature of the evidence), identify and analyse knowledge gaps, without in depth assessment of the quality of the studies included (Arksey & O'Malley, 2005; Munn et al., 2018; Tricco et al., 2018). This is in contrast to a systematic review where the aim is to draw firm conclusions or answers to a research question. Scoping reviews are a more suitable method of evidence synthesis where there is a need to understand the current state of the evidence in order to identify what further research is needed to advance knowledge on a given topic (Munn et al., 2018). We therefore conducted a scoping review to map the current literature on the association of MLTC with loneliness and social isolation and identify current gaps in the literature and limitations that are yet to be addressed.

2. Materials and method

2.1. Ethics

Ethical approval was not required for this study.

2.2. Approach

The scoping review was conducted in line with the five-stage framework outlined by Arksey and O'Malley (2005) and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Scoping Review (PRISMA-ScR) guidelines (Arksey & O'Malley, 2005; Tricco et al., 2018).

2.3. Search strategy

In April 2023, systematic electronic searches were conducted in six databases: Medline, Embase, CINAHL (EBSCOhost), The Cochrane Library, PsycInfo and Bielefeld Academic Search Engine (BASE). MeSH terms and keywords related to 'MLTC' or 'multimorbidity', 'loneliness', and 'social isolation' (identified through searching relevant systematic reviews) were used to search each database. Our search strategy included search terms used in the previous review (Hajek et al., 2020) as well as additional related terms to try and capture all relevant literature. Key terms for loneliness and social isolation were combined with Boolean operator 'OR' and 'AND' to capture studies on loneliness and MLTC or studies on social isolation and MLTC. Articles published from January 2020 to April 2023 were included to identify quantitative studies published since the previous systematic review. Search results were refined to include studies on humans and not restricted to any language. Detailed search terms for each database are available in Supplementary file 1. A hand search on Google based on the keywords was conducted to identify any additional literature. Any paper published before January 2020 that met our eligibility criteria and was not included in the previous systematic review were included here.

2.4. Eligibility criteria

Eligibility criteria were similar to the previous review by Hajek et al. (2020). Studies were eligible for inclusion if they assessed the association between MLTC and loneliness and/or social isolation in a human population (of any age), using measures that accurately captured each variable of interest (for example, the University of California at Los Angeles (UCLA) loneliness scale, the Lubben Social Network scale or relevant items from validated measures such as Center for Epidemiologic Studies Depression (CES-D) scale). Studies were excluded if they (a) did not include a precise measure of loneliness (e.g.: living alone, solitude), social isolation (e.g.: social exclusion) or MLTC, (b) focused on samples with a specific condition or specific outcomes, or (c) examined loneliness or social isolation during the COVID-19 lockdown.

2.5. Study selection

Search results were uploaded to Rayyan collaborative systematic review platform to allow rapid screening. Titles and abstracts were

blindly and independently screened against the eligibility criteria by two reviewers (HH, GS). Any discrepancies were resolved by discussion.

2.6. Data extraction and synthesis

Full text of potentially relevant articles were retrieved and reviewed independently by two reviewers (HH, GS). Data from included studies were extracted by one reviewer (HH) and verified by a second reviewer (GS). Data extracted were author name, publication date, country of study, population characteristics (specifically age, sex, and ethnicity where specified), sample size, study type, and key measures and findings. Extracted data were tabulated.

Data extracted from the review were grouped into two broad categories: (1) data on the association between MLTC and loneliness and (2) data on the association between MLTC and social isolation. A narrative synthesis approach was taken to summarise the data in each group (Popay et al., 2006). Specifically, the number of studies and overall findings within each group were summarised. Patterns, similarities and differences in findings were also described, with specific focus on studies using similar measures of loneliness/social isolation and MLTC.

3. Results

3.1. Search results

The results of the search strategy and selection process are shown in Fig. 1. 2616 citations were identified from the search. After deduplication, 1752 records were excluded at title and abstract screening. Seventy-five studies met the criteria for full text review, from which 58 were excluded. Reasons for exclusion are shown in Fig. 1. A total of 17 articles were selected for inclusion in the review.

3.2. Characteristics of included studies

Of the 17 studies, two studies were conducted in each of the US (Jang et al., 2022; Taylor, 2021), Germany (Hajek & König, 2021; Schübbe & König, 2023), and India (Ansari et al., 2023; Pengpid & Peltzer, 2021). One study was conducted in each of the UK, Switzerland, Canada, Thailand, Mexico, and Singapore (Atoyebi & Wister, 2017; Bevilacqua et al., 2022; Hämmig, 2019; Merchant et al., 2020; Pengpid & Peltzer, 2023; Pengpid & Peltzer, 2020). Five studies were multinational, with three focusing on the same cohort study in Europe and Israel (Cantarero-Prieto et al., 2018; Hajek & König, 2020; Sieber et al., 2023) and two focusing on a study in low- or middle-income countries (China, Ghana, India, Mexico, Russia, and South Africa) (Ma et al., 2021; Smith et al., 2022). Most studies were conducted in a community setting and used multi-stage sampling strategy to achieve representative samples. Almost all studies assessed adults (aged 18 years and over), with most focusing on older adults (aged 50 years and over). Sample size of studies ranged from 176 to 72,262 individuals. Twelve studies were cross-sectional and five were longitudinal cohort studies. Characteristics of the included studies are summarised in Tables 1 & 2.

Measurement of MLTC were all self-report of clinician-diagnosed conditions and covered a range of body systems (see Tables 1 & 2). Measurement of loneliness varied across studies in terms of number of questions (a single versus three-item measure) and recall period (ranging from yesterday to more generally). Measures of social isolation ranged from measures focusing on contact with family and friends to that including contact with any other people (e.g.: neighbours, acquaintances).

3.3. MLTC and loneliness

Eleven studies assessed the association between MLTC and loneliness

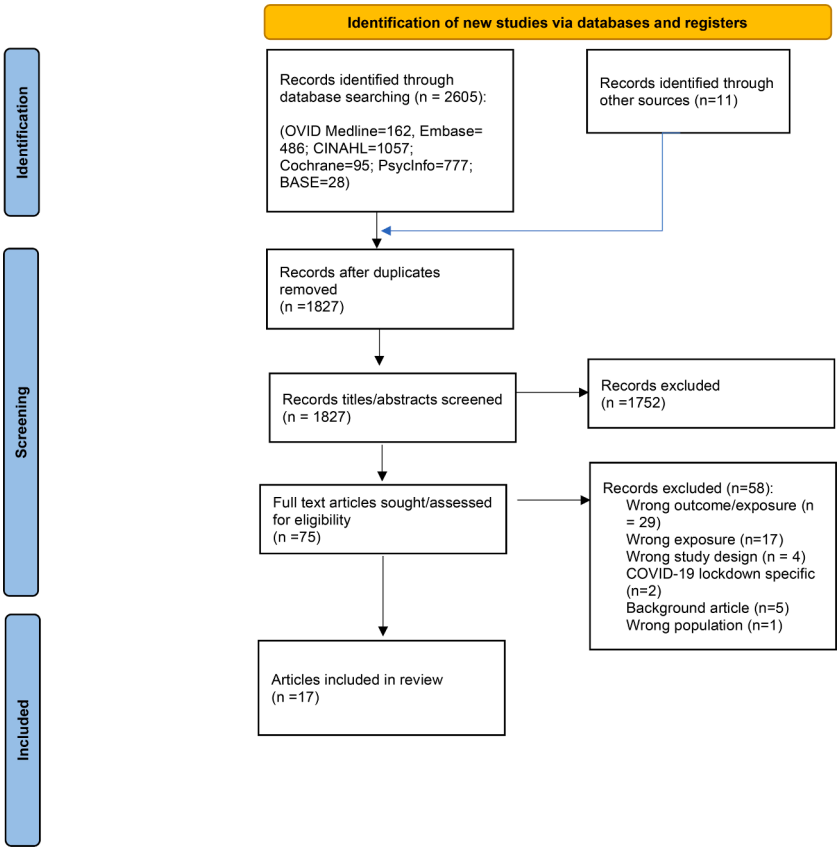

Fig. 1. Flow diagram illustrating screening process.

Table 1
Studies on the association between MLTC and loneliness*.

Author & Date	Country	Setting	Sampling strategy	Population Characteristics	Sample Size	Study Type	Study Aims	Loneliness measure	MLTC measure	Confounders adjusted for	Findings
Taylor et al., 2021	US	Households in the community	Complex multistage probability sampling design	African-American adults aged 50 and over	2323	Cross-sectional study	To study the impact of social isolation and loneliness on health and well-being	Hughes 3 item loneliness scale (How often do you feel you lack companionship? (b) How often do you feel left out, and (c) How often do you feel isolated from others?)	Self-report number of chronic conditions (physical and mental health): high blood pressure, diabetes, cancer, lung disease, heart problems, stroke, and arthritis	Gender, education, total household income, employment status, age, study wave	Loneliness was associated with number of chronic conditions.
Hajek et al., 2021	Germany	Private homes and institutionalized settings in NorthRhine-Westphalia (most populous state of Germany)	Multistage random sampling drawn from 94 communities in NorthRhine-Westphalia	Individuals aged 80 years and over	952	Cross-sectional study	To examine socioeconomic and health-related variables associated with psychosocial factors among the oldest old	A single item measure asking 'how often do you feel lonely?'. Responses ranging from 1=never/almost never to 4=always or almost always	Self report of 2 or more of 19 chronic diseases : myocardial infarction, heart failure, hypertension, stroke, mental illness, cancer, diabetes, respiratory or pulmonary disease, back pain, gastric or intestinal disease, kidney disease, liver disease, blood disease, joint or bone disease, bladder disease, sleep disorder, eye disease or visual disorder, ear disease or hearing impairment, and neurological disease	Sex, age group (80–84 years; 85–89 years; 90 years and over), marital status (married, living together with spouse; Other including married, living separated from spouse, widowed, divorced, and single), living situation (living in a private household; living in an institutionalized setting), educational level (ISCED-97[15] classification: low, medium, or high education), size of the social network, income poverty (threshold: 60 % of median household net equivalence income, in our study: 968 Euro) and asset poverty (0–2500 Euro), self-rated health (ranging from 1= very bad to 4= very good), functional impairment (IADL)	Multimorbidity was not associated with loneliness in models adjusting for sociodemographic and health variables
Schubbe et al., 2023	Germany	Private households	Two-stage stratified random sampling procedure	Adults (18 years and older)	44,385 observations	Longitudinal cohort study	To examine the longitudinal association between multimorbidity	The 3-item UCLA questionnaire: "How often do you miss the company of other people?", "How often	Self-report of 2 or more of 13 diseases: sleep disorder, diabetes, asthma,	Age, living situation (living alone or living together) and current unemployment (yes	Onset of multimorbidity is associated with an increase in loneliness in the total sample

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Table 1 (*continued*)

Author & Date	Country	Setting	Sampling strategy	Population Characteristics	Sample Size	Study Type	Study Aims	Loneliness measure	MLTC measure	Confounders adjusted for	Findings
							and loneliness in the general adult population (and in different age groups) in Germany.	do you feel left out?" and "How often do you feel socially isolated?" and rate them on a 5-point scale (1= "never", 2= "seldom", 3= "sometimes", 4= "often", 5= "very often").	cardiac disease (also cardiac insufficiency, weak heart), cancer, stroke, migraine, high blood pressure, depression, dementia, joint diseases (including arthritis, rheumatism), chronic back trouble and burnout	or no), self-rated health, satisfaction with household income,	and among individuals aged 65 years and older.
Ansari et al., 2023	India	Households in the community	Multi-stage, area probability cluster sampling design	Adults aged 60 years and over	31,464	Cross-sectional study	To examine multimorbidity as a risk factor for feelings of loneliness among older adults in India	A single-item measure was used focusing on the feeling of loneliness during the past week for which a question was asked to the respondents: During the past week, how often do you feel alone? The responses were 1, rarely or never (less than 1 day); 2, sometimes (1 or 2 days); 3, often (3 or 4 days); and 4, most or all of the time (5–7 days)	Self-report of 2 or more of 9 chronic health conditions: hypertension, chronic heart diseases, stroke, any chronic lung disease, diabetes, cancer or malignant tumor, any bone/joint disease, any neurological/ psychiatric disease, and high cholesterol	Age, sex, place or residence, marital status, living arrangement, education, smoking, alcohol use, activities of daily living, instrumental activities of daily living, self-rated health, financial support, physical activity.	Multimorbidity was associated with feeling lonely, both in unadjusted and adjusted models
Pengpid et al., 2022	India	Households in the community	Multistage stratified area probability cluster sampling	Adults aged 45 years and older	72,262	Cross-sectional study	To determine the prevalence and correlates of loneliness in middle-aged and older adults in India	Single item measure from the Center for Epidemiologic Studies Depression Scale (CES-d-10): 'How often did you feel alone in the past week?' Response options were coded into not feeling alone: 1= rarely or none of the time (<1 day), moderate feeling alone: 2= sometimes or 1–2 days/week and severe feeling alone: 3= occasionally or all the time or 3–7 days/ week)	Self-report of 2 or more of 9 conditions: 'hypertension or high blood pressure; diabetes or high blood sugar; cancer or malignant tumour; chronic lung disease such as asthma, chronic obstructive pulmonary disease/chronic bronchitis or other chronic lung problems; chronic heart diseases such as	Education (none and ≥1 years), age, sex (male, female), marital status (currently married vs. widowed/ divorced/ separated/deserted/ live-in relationship/ never married), urban and rural residence, subjective socioeconomic status, intrinsic religiosity, organizational religiosity, social participation	Multimorbidity was positively associated with severe loneliness

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Table 1 (*continued*)

Author & Date	Country	Setting	Sampling strategy	Population Characteristics	Sample Size	Study Type	Study Aims	Loneliness measure	MLTC measure	Confounders adjusted for	Findings
									coronary heart disease (heart attack or myocardial Infarction), congestive heart failure, or other chronic heart problems; stroke; arthritis or rheumatism, osteoporosis or other bone/joint diseases; any neurological, or psychiatric problems such as depression, Alzheimer's/ dementia, unipolar/bipolar disorders, convulsions, Parkinson's etc.; high cholesterol		
Atoyebi et al. 2017	Canada	Community	Multi-stage sample allocation strategy	Individuals aged 80 years and over	6427	Cross-sectional study	To examine the association between multimorbidity and loneliness and whether this is mediated by pain	Not available	Self-report 14 conditions: joint pain, asthma, chronic obstructive pulmonary disease, sleep apnea, scoliosis, fibromyalgia, arthritis, osteoporosis, high blood pressure, heart disease, stroke, diabetes, cancer and mood disorder (i.e. depression, bipolar, mania, dysthymia)	Age, sex, marital status, education, income, perceived pain, functional status	Multimorbidity modestly increases the risk of loneliness among older persons and perceived pain appears to slightly mediate this effect
Pengpid et al., 2023	Thailand	Households in the community	National multi-stage sampling (regions, provinces, blocks or villages, households)	Adults aged 45 years and older	3696	Longitudinal study	To investigate the prevalence and associated factors of incident and persistent loneliness in a prospective cohort study among ageing adults	A single item from the "Center for Epidemiologic Studies Depression (CES-d-10) scale," "In the past week, how often did you experience feeling lonely?" defined as "almost always (5–7 days),	Self-report of 2 or more of 12 conditions: hypertension, diabetes, vascular diseases/heart disease/heart failure, rheumatism/ arthritis, bone	Marital status, highest level of education, sex, age, region, religion, and personal annual income, substance use, physical activity, body mass index (BMI), activities of daily	Having three or more chronic conditions (aOR: 1.76, 95 % CI: 1.19 to 2.60) were positively associated with incident loneliness (2 years later); having three or more chronic diseases (aOR: 1.78, 95 % CI:

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Table 1 (*continued*)

Author & Date	Country	Setting	Sampling strategy	Population Characteristics	Sample Size	Study Type	Study Aims	Loneliness measure	MLTC measure	Confounders adjusted for	Findings
							(≥ 45 years) in Thailand	often (3–4 days) or sometimes (1–2 days)"=1 and "very rarely (less than one day) or none"=0.	diseases/low bone density/ osteoporosis, kidney diseases, lung diseases/ emphysema, cancer, liver diseases, brain diseases/ Alzheimer's disease, visual impairment, hearing impairment.	living disability, history of accidents, fear of falling with activity avoidance, self-rated physical health status, depressive symptoms.	1.07 to 2.98) were positively associated with persistent loneliness
Pengpid et al., 2020	Mexico	Households in the community	Stratified multistage cluster sampling design	Older adults (aged 50 years and over)	3903	Cross-sectional study	To determine the prevalence and correlates of loneliness in older Mexicans	Single item measure - 'Did you feel lonely for much of the day yesterday?'	Self-report of 2 or more of 11 conditions: angina, arthritis, asthma, chronic back pain, chronic lung disease, diabetes, edentulism, hearing problems, hypertension, stroke, visual impairment	Educational level, age, sex, marital and residence status, wealth quartiles, social engagement, trust, unsafe environment, childhood health status, physical activity, high-risk alcohol use, tobacco use.	In adjusted logistic regression analysis, multimorbidity was positively and being married or cohabiting and higher wealth status were negatively associated with loneliness.
Hajek et al., 2020	Europe and Israel	Private households	Sampling varies across countries	Individuals aged 50 years and over	101,909 observations	Longitudinal cohort study	To clarify which factors are associated with loneliness longitudinally based on nationally representative data	3 item UCLA questionnaire: "How often do you feel isolated from others?", "How often do you feel you lack companionship?", "How often do you feel left out?"	Self-report of 2 or more of 11 conditions: high blood pressure or hypertension; high blood cholesterol; stroke or cerebral vascular disease; diabetes or high blood sugar; chronic lung disease; arthritis, including osteoarthritis, or rheumatism; cancer or malignant tumor; stomach or duodenal ulcer, peptic ulcer; Parkinson's disease; cataracts; hip fracture or femoral fracture	Age, marital status, income, self-rated health, functional decline, depressive symptoms, cognitive functioning	Changes in loneliness was not associated with changes in number of chronic conditions

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Table 1 (*continued*)

Author & Date	Country	Setting	Sampling strategy	Population Characteristics	Sample Size	Study Type	Study Aims	Loneliness measure	MLTC measure	Confounders adjusted for	Findings
Sieber et al., 2022	Europe and Israel	Private households	Sampling varies across countries	Individuals aged 50 years and over	37,082	Longitudinal cohort study	To examine multiple potential mediating factors (loneliness, Activities of Daily Living [ADL], Instrumental Activities of Daily Living [IADL], depressive symptoms) in the relationship between multimorbidity and quality of life	3-item UCLA questionnaire: "How often do you feel isolated from others?", "How often do you feel you lack companionship?", "How often do you feel left out?"	Self-report of 2 or more of 11 conditions: high blood pressure or hypertension; high blood cholesterol; stroke or cerebral vascular disease; diabetes or high blood sugar; chronic lung disease; arthritis, including osteoarthritis, or rheumatism; cancer or malignant tumor; stomach or duodenal ulcer, peptic ulcer; Parkinson's disease; cataracts; hip fracture or femoral fracture	Gender, highest educational attainment (time invariant) and time varying: age, country of residence, employment status (employed, unemployed, retired, and out of the labour force), partnership status (alone and partnered), household financial strain, pain, number of observations per respondent.	At baseline, people with multimorbidity were more lonely (statistically significant). Multimorbidity (at baseline) was associated with lower QoL (assessed 4 years later) but this was not mediated by loneliness (Assessed two years later)
Smith et al., 2022	China, Ghana, India, Mexico, Russia, and South Africa	Households in the community	A multistage clustered sampling design	Adults aged 50 years and over	34,129	Cross-sectional study	To assess the association between physical multimorbidity (i.e., ≥2 chronic physical conditions) and depression among older adults, and explore mediators of the association	Single item measure- "Did you feel lonely for much of the day yesterday?" with answer options "yes" or "no.	Self-report of 2 or more of 11 chronic physical conditions (angina, arthritis, asthma, chronic back pain, chronic lung disease, diabetes, edentulism, hearing problems, hypertension, stroke, and visual impairment)	Age, sex, years of education received, marital status, and smoking	Older adults with physical multimorbidity are at increased odds of depression in LMICs and this association is mediated by loneliness.

* Reference numbers in brackets.

Table 2
Studies on the association between MLTC and social isolation*.

Author and Year	Country	Setting	Sampling strategy	Population Characteristics	Sample Size	Study Type	Study Aims	Social isolation measure	MLTC measure	Confounders	Findings
Jang et al., 2021	US	Households in the community	Convenience sampling approach	Asian Americans aged 18 or above living in the Austin area	2609	Cross-sectional study	To examine the factors associated with social isolation in Asian Americans	Lubben Social Network Scale–6; includes three items on family and a similar set of three items on friends: (How many relatives do you see or hear from at least once a month? How many relatives do you feel at ease with that you can talk about private matters? How many relatives do you feel close to such that you could call on them for help?),	Self-report of 2 or more of 10 chronic medical conditions (diabetes, cancer, arthritis, heart disease, high blood pressure, stroke, liver disease, kidney problem, asthma, and chronic obstructive pulmonary disease)	Age, gender, ethnic origin, marital status, education, and perceived financial status), self-rated health, and immigration-related (proportion of life in the United States and English proficiency) variables	Number of chronic conditions (0, 1, 2 or more) was not significantly associated with overall social isolation or social isolation from friends and family.
Taylor et al., 2021	US	Households in the community	Complex multistage probability sampling design	African-American adults aged 50 and over	2323	Cross-sectional study	To study the impact of social isolation and loneliness on health and well-being	Social network index (8-item measure-having less than once a month social contact with adult children, less than once a month contact with other family members, and less than once a month contact with friends, being unmarried, living alone, having no participation in social groups or social activities, and having no religious service attendance	Self-report number of chronic conditions (7 conditions: high blood pressure, diabetes, cancer, lung disease, heart problems, stroke, and arthritis)	Gender, education, total household income, employment status, age, study wave	Social isolation was not associated with number of chronic conditions
Bevilacqua et al., 2022	UK	Households in the community	Men and women whose birth and infant data were recorded in historical ledgers by midwives and health visitors were traced	Men and women born in Hertfordshire between 1920 and 30 and still living there in the early 1990s	176	Cross-sectional study	To examine the association between number of chronic non-communicable disease and social isolation in a cohort of community-dwelling older adults in the UK, and to consider whether any potential association is mediated by frailty.	6-item Lubben Social Network Scale (LSNS-6), measures the number and frequency of social interactions with friends (three items) and family members (three items: How many relatives do you see or hear from at least once a month? How many relatives do you feel at ease with that you can talk about private matters? How many	Number of chronic conditions: Have you been told by a doctor that you have any of the following conditions?'. The following conditions were recorded: high blood pressure, diabetes, lung disease (asthma, COPD, emphysema, chronic bronchitis),	Age, BMI, social class, marital status, smoker status, alcohol consumption, frailty	A greater number of NCDs was associated with higher odds of being isolated in women in the unadjusted model (OR per additional NCD 1.65, 95 % CI 1.08, 2.52, p = 0.021). This association persisted after adjustment for confounders, i.e. age, BMI, social class, marital status, smoker status and

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Table 2 (*continued*)

Author and Year	Country	Setting	Sampling strategy	Population Characteristics	Sample Size	Study Type	Study Aims	Social isolation measure	MLTC measure	Confounders	Findings
								relatives do you feel close to such that you could call on them for help?))	rheumatoid arthritis, multiple sclerosis, cancer, vitiligo, depression, Parkinson's disease, heart disease (heart attack, angina, heart failure), peripheral arterial disease (claudication), osteoporosis, thyroid disease, and stroke		alcohol consumption (OR 1.93, 95 % CI 1.11, 3.34, p = 0.020), and it remained robust when Fried frailty was added to the model (OR 1.85, 95 % CI 1.06, 3.22, p = 0.031).
Hammig et al., 2019	Switzerland	Private households	Stratified, multistage random sampling	Adolescents (aged >15 years) and adults	21,597	Cross-sectional study	To examine prevalence rates and associations of social isolation with various health conditions and behaviours in the entire Swiss population and across different age groups	A score of social disconnectedness derived from 3 questions: number of related persons to count on, number of confidants among related persons, concern and empathy by other people in what one is doing. A score of perceived isolation derived from: regretting the absence of a confidant, feelings of loneliness (from never to very often).	Self-report; 3 or more of 10 general, physical and mental health problems, as well as chronic (back, neck and shoulder, stomach, chest) pain, strong headaches, strong tachycardia or palpitation, and moderate to severe depression	Sex, age and education, foreign nationality and overweight/ obesity (BMI >25)	The socially isolated people independent of their age showed strongly elevated relative risks of poor self-rated health (aOR= 4.0), musculoskeletal disorders (aOR= 2.8), moderate to severe depression (aOR= 11.5), and multiple health problems (aOR= 5.0).
Merchant et al., 2020	Singapore	Households in the community	Recruitment through network of grassroots volunteers, senior activity centres and words of peers who attended the screening program intended to identify seniors at risk, e.g., pre-frail, frail and those with cognitive impairment	Older adults aged 60 years and older	202	Cross-sectional study	To determine the prevalence of social isolation and its association with gait speed, frailty, cognition, depression and comorbidities amongst community-dwelling older adults	6-item Lubben Social Network Scale (LSNS-6), measures the number and frequency of social interactions with friends (three items) and family members (three items)	Number of chronic diseases	Age, sex, marital status, education, social network size, activity score, number of technologies in use, self-rated health, functional impairment, depressive symptoms, cognitive impairment	Number of chronic diseases was significantly associated with social isolation, in both unadjusted (1.21(0.97–1.51)) and adjusted models (1.22 (0.96–1.54))
Cantarero-Prieto et al., 2018	Europe and Israel	Private households	Sampling varies across countries	Individuals aged 50 years and over	37,864	Longitudinal cohort study	To examine whether there is an increase in the	Social isolation measured using 3 proxies: (1) living	Self-report of 2 or more of 11 conditions: high	Quality of life, gender, age, educational	People with greater social participation have lower risk of

(*continued on next page*)

Table 2 (*continued*)

Author and Year	Country	Setting	Sampling strategy	Population Characteristics	Sample Size	Study Type	Study Aims	Social isolation measure	MLTC measure	Confounders	Findings
							propensity of being diagnosed with chronic illnesses because of a decrease in social relations for elderly Europeans	alone, (2) whether activities of the individual during the last month include providing help to family, friends or neighbours, and (3) whether activities for individuals in the previous month include going to sports, social or other clubs.	blood pressure or hypertension; high blood cholesterol; stroke or cerebral vascular disease; diabetes or high blood sugar; chronic lung disease; arthritis, including osteoarthritis, or rheumatism; cancer or malignant tumor; stomach or duodenal ulcer, peptic ulcer; Parkinson's disease; cataracts; hip fracture or femoral fracture	level, employment status, geographic characteristics	suffering from multiple chronic diseases.
Ma et al., 2021	China, Ghana, India, Mexico, Russia, and South Africa	Households in the community	A multistage clustered sampling design	Adults aged 65 years and over	14,585	Cross-sectional study	To investigate the relationship between physical multimorbidity and social participation among older adults across 6 LMICs	Index based on 9 questions on the participant's involvement in community activities in the past 12 months (e.g., attended religious services, club, society, union, etc.)	Self-report of 3 or more of 11 chronic physical conditions (angina, arthritis, asthma, chronic back pain, chronic lung disease, diabetes, edentulism, hearing problems, hypertension, stroke, and visual impairment)	Age, sex, wealth, education, marital status, living arrangement, BMI, physical activity, smoking, alcohol consumption, loneliness, depression, and country,	Overall, an increasing number of chronic conditions was dose-dependently associated with lower levels of social participation (e.g., ≥4 vs 0 conditions: $\beta = -0.26$ [95 % CI = −0.39, −0.13]). The association was more pronounced among males than females.

* Reference numbers in brackets.

(Ansari et al., 2023; Atoyebi & Wister, 2017; Hajek & König, 2021; Hajek & König, 2020; Pengpid & Peltzer, 2021; Pengpid & Peltzer, 2023; Pengpid & Peltzer, 2020; Schübbe & König, 2023; Sieber et al., 2023; Smith et al., 2022; Taylor, 2021). Eight were cross-sectional studies (Ansari et al., 2023; Atoyebi & Wister, 2017; Hajek & König, 2021; Pengpid & Peltzer, 2021; Pengpid & Peltzer, 2020; Sieber et al., 2023; Smith et al., 2022; Taylor, 2021) and three were longitudinal studies (Hajek & König, 2020; Pengpid & Peltzer, 2023; Schübbe & König, 2023).

3.3.1. Evidence from studies using single-item measures of loneliness

Two cross-sectional studies, based on the same dataset (Ansari et al., 2023; Pengpid & Peltzer, 2021), assessed loneliness using a single question of "during the past week, how often did you feel alone?" and MLTC as defined as presence of ≥2 of 9 specified conditions. Both studies reported that loneliness was significantly associated with MLTC, both for adults aged ≥45 years and adults aged ≥60 years living in India. Both studies adjusted for similar demographic variables, though one additionally adjusted for health behaviour variables (Ansari et al., 2023) while the other additionally adjusted for religiosity and social participation (Pengpid & Peltzer, 2021) (Table 1). One longitudinal study reported that MLTC (defined as presence of > 2 of 12 specified conditions) was associated with incident (newly-occurring) loneliness (measured using the same single question) two years later in 3696 adults (aged ≥45 years old) in Thailand (Pengpid & Peltzer, 2023). The latter study included a wider range of conditions (specifically, visual impairment, hearing impairment, kidney, and liver disease) in their assessment of MLTC, but also adjusted for sociodemographic and health behaviour variables.

Two further studies reported a significant cross-sectional association between loneliness (measured using a single question: "did you feel lonely for much of the day yesterday?") and MLTC (defined as the presence of ≥2 of the same 11 conditions) in adults aged ≥50 years living in Mexico (Pengpid & Peltzer, 2020) and China, Ghana, India, Mexico, Russia, and South Africa (Smith et al., 2022). Both studies controlled for similar sociodemographic variables, while the former study additionally adjusted for social engagement, environment, childhood health status and health behaviour variables.

One cross-sectional study, based on a relatively small sample of 952 individuals aged 80 years and over and using a slightly different measure of loneliness- 'how often you feel lonely?", did not find a significant association between MLTC (defined as presence of ≥2 of 19 specified conditions) and loneliness (Hajek & König, 2021). This study adjusted for a similar set of confounders as some of the cross-sectional studies (Table 1).

3.3.2. Evidence from studies using a three-item measure of loneliness

Four studies (Hajek & König, 2020; Schübbe & König, 2023; Sieber et al., 2023; Taylor, 2021) assessed loneliness using 3 questions that asked participants to rate (a) how often they lacked companionship, (b) how often they felt let out, and (c) how often they felt socially isolated. Of these studies, one reported a significant cross-sectional association between loneliness and MLTC (defined as presence of ≥2 of 9 chronic conditions) in African-American adults aged ≥50 years old (Taylor, 2021). This study controlled only for sociodemographic variables. Together, two longitudinal studies (Hajek & König, 2020; Sieber et al., 2023) based on the same dataset and using the same definition of MLTC (≥2 of the same 11 conditions) reported that, in adults aged ≥50 years old living in Europe and Israel, MLTC was associated with higher odds of incident loneliness two years later but there was no significant association between changes in MLTC and changes in loneliness over time. These studies adjusted for different confounders and used different analytical models. A separate longitudinal study explored changes in levels of loneliness and MLTC (defined as presence of ≥2 of 13 specified conditions) over time and found that an increase in levels of loneliness was associated with the onset of MLTC (Schübbe & König, 2023). However, this study did not control for key confounders such as sex, marital status, educational attainment (Schübbe & König, 2023).

3.4. MLTC and social isolation

Seven studies examined the association between MLTC and social isolation (Bevilacqua et al., 2022; Cantarero-Prieto et al., 2018; Hämmig, 2019; Jang et al., 2022; Ma et al., 2021; Merchant et al., 2020; Taylor, 2021). Six were cross-sectional studies (Table 2).

Three cross-sectional studies assessed social isolation using the 6-item Lubben Social Network scale (Bevilacqua et al., 2022; Jang et al., 2022; Merchant et al., 2020). Of these studies, one was a US study focusing on Asian Americans and reported that social isolation was not associated with MLTC (Jang et al., 2022). In contrast, one study each in the UK and in low- and middle-income countries, found a significant association between social isolation and MLTC in older adults (Bevilacqua et al., 2022; Merchant et al., 2020). However, each of these studies used different conditions in their assessment of MLTC, and adjusted for different confounders, making direct comparisons difficult.

Similarly, the remaining four studies each used different measures of social isolation, varied assessments and definitions of MLTC (some defining MLTC as ≥2 conditions, while others defined MLTC as ≥3 conditions), and adjusted for different confounders. Of these studies, one assessed the association in both adolescents (aged ≥15 years) and adults and found that socially isolated people (regardless of age) were more likely to have MLTC (Hämmig, 2019), though this study did not control for key confounders such as smoking, and alcohol consumption. One study in low- and middle-income countries, found a significant association between social isolation and MLTC in older adults (Ma et al., 2021). Ma et al. (2021) further reported that the association between MLTC and social isolation was stronger for men than women (Ma et al., 2021). One US study on African Americans reported that social isolation was not associated with MLTC in their study (Taylor, 2021), though they did not adjust for health behaviours. Using multiple observations on social isolation and MLTC collected over 11 years, Cantarero-Preieto et al. (2018) found that, at multiple time points, people with greater social participation were less likely to have MLTC (Cantarero-Prieto et al., 2018). However, this study did not adjust for health behaviours.

4. Discussion

4.1. Main findings of this study

This scoping review allowed us to rapidly collate the emerging evidence on the association between loneliness, social isolation, and MLTC. Overall, our review identified some further evidence for a cross-sectional association of MLTC with loneliness. Findings from studies on the association between MLTC and social isolation and longitudinal studies on the association between MLTC and loneliness were more mixed, making the nature of these associations less clear. These studies were heterogenous in terms of measures and definitions of loneliness/social isolation and MLTC, confounders adjusted for and analytical models used, making comparisons difficult. Further population-based longitudinal studies using similar measures and methodological approaches (and examining independent effects of both loneliness and social isolation) are needed to better understand the nature of these relationships.

4.2. What is already known on this topic

The systematic review by Hajek et al. (2020) was based on studies conducted in European and Canadian populations and indicated that loneliness is associated with MLTC (Hajek et al., 2020). A more recent multi-country systematic review did not focus specifically on loneliness

and social isolation but suggested that reduced social networks increased risk of MLTC, while having a large social network was protective of MLTC (Álvarez-Gálvez et al., 2023). Both of these reviews were based on only a few studies and recommended further research to improve understanding of these associations. Further studies on this topic have now been published. However, to the best of our knowledge, there is no review that collates this current evidence.

4.3. What this study adds

This scoping review identified 17 additional studies on the link between loneliness, social isolation and MLTC since the last systematic review was published, including longitudinal studies and studies in low- and middle-income countries (LMICs). This review found that the current evidence largely suggests an important cross-sectional association of MLTC with loneliness, but weaker evidence for a longitudinal association between MLTC and loneliness and MLTC with social isolation.

To some extent, differences in study findings may be due to varying definitions of MLTC (e.g., presence of $\geq$2 vs $\geq$3 conditions) and the use of different combinations of long-term conditions to assess MLTC. Previous studies have illustrated differential associations between loneliness/social isolation and long-term conditions (Hong et al., 2023). It is plausible that studies that included a larger number of cardiovascular-related long-term conditions or did not include functional impairment in their definition of MLTC, for example, may be less likely to report a significant association between loneliness and MLTC. Similarly, studies used different measures for loneliness/social isolation which may contribute to inconsistent findings. Different measures may capture different aspects of each construct and perform differently in different populations and study designs (Office for National Statistics). Single measures may be also more susceptible to measurement error and sociopsychological bias, therefore reducing their reliability (Allen et al., 2022). A further explanation for inconsistent findings is the use of different methodological approaches to examine longitudinal association between MLTC. This includes different study sample sizes, adjustment for different confounders and also different analytical models used. For example, some studies explored the association between concurrent changes in MLTC and loneliness (adjusting for person-specific unobserved confounders (Hajek & König, 2020; Schübbe & König, 2023)), while some studies examined prospective associations between these variables (Hämmig, 2019; Pengpid & Peltzer, 2023; Sieber et al., 2023). However, it is possible that the association between MLTC and loneliness or social isolation varies across different age, sex, or ethnic and cultural groups. For example, people from ethnic minority groups may have different behaviours in and expectations of social relationships due to socio-cultural factors. Measurements of social isolation (and loneliness) may also perform differently for ethnic minorities as they often do not account for ethnic and cultural differences (Lewis & Cotterell, 2018; Victor et al., 2012; Victor et al., 2020). As a result, people from ethnic minority groups may interpret these measures differently, which may result in inaccurate responses.

This current review also highlighted a lack of studies on the longitudinal association between MLTC and social isolation, emphasising the need for studies in this area. It is not clear why there are fewer studies on social isolation, though this may reflect the availability of population-based cohort studies that include validated measures of social isolation. It is important to understand how social isolation relates to MLTC over time, particularly in older adults who may experience shifts in their social network and may no longer have the social resources to manage their health (Breckner et al., 2021; Corbett et al., 2022; Hissa et al., 2020). Finally, there was only one study that reported on independent associations of loneliness and social isolation (adjusting for one another) with MLTC in the same study population. The cross-sectional study found that MLTC was associated with loneliness but not social isolation in 2323 African–Americans living in the United States. Their study may suggest that mechanisms through which loneliness relates to MLTC may be more important than other mechanisms through which social isolation may relate to MLTC (Taylor, 2021). Social isolation may influence MLTC due to several mechanisms: reduced access to basic needs (i.e., food, hygiene) and healthcare [instrumental support], reduced access to information about healthcare and management of conditions [informational support], reduced interaction with people who can promote healthier lifestyle and act as stress-buffers [behavioural support] (Shankar et al., 2011). Reduced social interaction may also result in changes in neural functioning and cognitive impairment (White et al., 2015). Loneliness – the subjective feeling of alienation- may influence MLTC due to psychological processes including perception of reduced social support during stressful situations and reduced perceived ability to navigate or recover from stressful events (Bhatti & Haq, 2017; Hong et al., 2023). These cognitive appraisals may result in harmful health behaviours (e.g., heavy drinking, smoking) and also activate the hypothalamic–pituitary–adrenal (HPA) axis which results in production of hormones. Overproduction of these hormones have been implicated in the development of long-term conditions (Bhatti & Haq, 2017). However, further studies should examine associations of MLTC with both loneliness and social isolation, using measures that have been evaluated for a given population, to disentangle the mechanisms through which they influence MLTC. This includes a need for qualitative studies to improve our understanding of potential mechanisms underlying these relationships. This understanding would inform interventions aimed at targeting loneliness and/or social isolation or delaying multimorbidity.

4.4. Strengths and limitations of the study

Strengths of this study include the use of a systematic approach to identify relevant studies from multiple databases and screening of studies by two reviewers. However, it is possible that some relevant studies were not captured as search results were limited to those in the English language. Although we used multiple key terms for our variables of interest, any relevant studies that did not label their study using these terms will have been excluded. We also excluded studies that examined the association between MLTC and loneliness/social isolation during the COVID-19 lockdown or studies that examined associations with comorbid loneliness and depression or MLTC with frailty (Liu et al., 2021). We excluded studies assessing association between closely-related but distinct measures (Xu et al., 2023) or studies that described differences between levels of loneliness in people living with MLTC compared to those without MLTC (Makovski et al., 2020). Further, quality appraisal of studies was not conducted as this is not a requirement of scoping reviews. However, we note that most studies used cross-sectional designs and may be susceptible to reverse causality and most studies used self-report measures which may be limited by recall or social desirability bias. Our searches identified that most studies focused on older populations, highlighting a lack of studies on younger adults. There were no studies that explored possible bidirectional associations between MLTC and loneliness and/or social isolation. Bidirectional associations may exist since people with MLTC often experience loneliness and/or social isolation and experiencing social isolation and loneliness have been linked to worse outcomes in people with MLTC (Calderón-Larrañaga et al., 2018; Cantarero-Prieto et al., 2018; Olaya et al., 2017). Identifying possible bidirectional associations could shed light on the nature of the association. Finally, we were unable to make direct comparisons across studies, due to the use of different measures of loneliness/social isolation, definitions of MLTC, differences in study population and size, as well as study design and statistical approaches.

5. Conclusion

Further population-based longitudinal studies using similar measures and consistent methodological approaches are needed to improve understanding of the longitudinal association of MLTC with both loneliness and social isolation. Such studies may also examine the direction

of any association between MLTC and loneliness and social isolation, and whether this association varies for certain subgroups.

Data availability

No new data were generated or analysed in support of this research.

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CRediT authorship contribution statement

Hilda Hounkpatin: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Glenn Simpson:** Writing – review & editing, Investigation, Formal analysis. **Miriam Santer:** Writing – review & editing. **Andrew Farmer:** Writing – review & editing. **Hajira Dambha-Miller:** Writing – review & editing.

Declaration of competing interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.archger.2024.105347.

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